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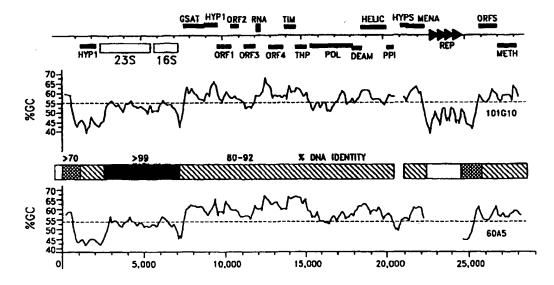
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(54) Title: NUCLEIC ACIDS AND PROTEINS FROM CENARCHAEUM SYMBIOSUM



(57) Abstract

The present application relates to nucleic acids and polypeptides from Cenarchaeum symbiosum. Methods of making the polypeptides and antibodies against the polypeptides are also described.

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NUCLEIC ACIDS AND PROTEINS FROM CENARCHAEUM SYMBIOSUM

Background of the Invention

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The identification and characterization of organisms which inhabit a diverse range of ecosystems leads to a greater understanding of the operation of such ecosystems. In addition, because the physiology of such organisms is adapted to function in the particular habitat which the organism inhabits, the enzymes which carry out the organism's physiological processes may possess characteristics which provide advantages when they are utilized in therapeutic procedures, industrial applications, or research applications. Furthermore, by determining the sequences of these organisms' genes, insight into their biochemical pathways and processes may be gained without the necessity of culturing the organisms in the laboratory, thereby enabling the physiological characterization of organisms which are recalcitrent to growth in the laboratory.

Molecular phylogenetic surveys have recently revealed an ecologically widespread Crenarchaeal group that inhabits cold and temperate terrestrial and marine environments. To date these organisms have resisted isolation in pure culture, so their phenotypic and genotypic characteristics remain largely unknown. In order to characterize the physiology of these archaea, to develop methodological approaches for characterizing uncultivated microorganisms and identifying their presence in a sample, and to identify enzymes produced by these archae which may be useful in therapeutic, industrial, or laboratory applications, genomic analyses of the non-thermophilic crenarchaeote Cenarchaeum symbiosum was undertaken.

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Non-thermophilic Crenarchaeota are one of the more abundant, widespread and frequently recovered prokaryotic groups revealed by molecular phylogenetic approaches. These microorganisms were originally detected in high abundance in temperate ocean waters and polar seas. (DeLong, E. F. 1992. Archaea in coastal marine environments, Proc. Natl. Acad. Sci. 89, 5685-5689; DeLong, E. F et al. 1994. High abundance of Archaea in Antarctic marine picoplankton. Nature 371, 695-697; Fuhrman, J. A., et al. Davis. 1992. Novel major archaebacterial group from marine plankton. Nature 356, 148-149; Massana, R., et al. 1997. Vertical distribution and phylogenetic characterization of marine planktonic Archaea in the Santa Barbara Channel. Appl. Env. Microb. 63, 50-56; McInerney, J.O. et al. 1995. Recovery and phylogenetic analysis of novel archaeal rRNA sequences from a deep-sea deposit feeder. Appl. Env. Microb. 61, 1646-1648; Preston, C. M. et al. 1996. A psychrophilic crenarchaeon inhabits a marine sponge: Cenarchaeum symbiosum gen. nov., sp. nov. Proc. Natl. Acad. Sci. USA 93, 6241-6246) Representatives have now been reported in terrestrial environments and freshwater lake sediments, indicating a widespread distribution. (Bintrim, S.B. et al. 1997. Molecular phylogeny of Archaea from soil. Proc. Natl. Acad. Sci. USA 94, 277-282; Jurgens, G. et al. 1997. Novel group within the kingdom Crenarchaeota from boreal forest soil. Appl. Env. Mircob. 63, 803-80515, Kudo, Y. et al. 1997. Peculiar archaea found in Japanese paddy soils. Biosc. Biotech. Biochem. 61, 917-920; Ueda, et al. 1995. Molecular phylogenetic analysis of a soil microbial community. Eur. J. Soil Sci. 46, 415-421; Hershberger, K. L. et al. 1996. Wide diversity of Crenarchaeota. Nature 384, 420;

MacGregor, B.J. 1997. Crenarchaeota in Lake Michigan sediment. *Appl. Env. Microb.* 63, 1178-1181 *et al.*; Schleper, C.*et al.* 1997. Recovery of crenarchaeotal ribosomal DNA sequences from freshwater-lake sediments. *Appl. Env. Microb.* 63, 321-323) The ecological distribution of these organisms was initially surprising, since their closest cultivated relatives are all thermophilic or hyperthermophilic. No representative of this new archaeal group has yet been obtained in pure culture, so the phenotypic and metabolic properties of these organisms, as well as their impact on the environment and global nutrient cycling, remain unknown. Since growth temperature and habitat characteristics vary so widely between non-thermophilic and the hyperthermophilic *Creanarchaeota*, these groups are likely to differ greatly with respect to their specific physiology and metabolism.

To gain a better perspective on the genetic and physiological characteristics of non-thermophilic crenarchaeotes, a genomic study of *Cenarchaeum symbiosum* was begun. This archaeon lives in specific association with the marine sponge *Axinella mexicana* off the coast of California, allowing access to relatively large amounts of biomass from this species. (Preston, C. M. *et al.* 1996. A psychrophilic crenarchaeon inhabits a marine sponge: Cenarchaeum symbiosum gen. nov., sp. nov. *Proc. Natl. Acad. Sci.* USA **93**, 6241-6246) The approach taken herein differs in several respects from now standard genomic characterization of cultivated organisms, and also from comparable studies of uncultivated obligate parasites or symbionts. *C. symbiosum* has not been completely physically separated from the tissues of its metazoan host. Therefore, its genetic material needs to be identified within the context of complex genomic libraries that contain significant amounts of eucaryotic DNA, as well as DNA derived from members of *Bacteria*.

Molecular phylogenetic surveys of mixed microbial populations have revealed the existence of many new lineages undetected by classical microbiological approaches. (DeLong, E. F. 1997. Marine microbial diversity: the tip of the iceberg. *Tibtech* 15, 2-9.; Pace, N. R. 1997. A molecular view of microbial diversity and the biosphere. *Science* 276, 734-740) Furthermore, quantitative rRNA hybridization experiments demonstrate that some of these novel prokaryotic groups represent major components of natural microbial communities. These molecular phylogenetic approaches have altered current views of microbial diversity and ecology, and have demonstrated that traditional cultivation techniques may recover only a small, skewed fraction of naturally occurring microbes. However, phylogenetic identification using single gene sequences provides a limited perspective on other biological properties, particularly for novel lineages only distantly related to cultivated and characterized organisms. Consequently, additional approaches are necessary to better characterize ecologically abundant and potentially biotechnologically useful microorganisms, many of which resist cultivation attempts.

Summary of the Invention

One embodiment of the present invention is an isolated, purified, or enriched nucleic acid comprising a sequence selected from the group consisting of SEQ ID NO: 1 and SEQ ID NO: 2, the sequences complementary to SEQ ID NO: 1 and SEQ ID NO: 2, fragments comprising at least 10 consecutive nucleotides of SEQ ID NO: 1 and SEQ ID NO: 2, and fragments comprising at least 10 consecutive nucleotides of the sequences complementary to SEQ ID NO: 1 and SEQ ID NO: 2. One aspect of the present invention is an isolated, purified, or enriched nucleic acid capable of

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hybridizing to the nucleic acid of this embodiment under conditions of high stringency. Another aspect of the present invention is an isolated, purified, or enriched nucleic acid capable of hybridizing to the nucleic acid of this embodiment under conditions of moderate stringency. Another aspect of the present invention is an isolated, purified, or enriched nucleic acid capable of hybridizing to the nucleic acid of this embodiment under conditions of low stringency. Another aspect of the present invention is an isolated, purified, or enriched nucleic acid having at least 70% homology to the nucleic acid of this embodiment as determined by analysis with BLASTN version 2.0 with the default parameters. Another aspect of the present invention is an isolated, purified, or enriched nucleic acid having at least 99% homology to the nucleic acid of this embodiment as determined by analysis with BLASTN version 2.0 with the default parameters.

Another embodiment of the present invention is an isolated, purified, or enriched nucleic acid comprising a sequence selected from the group consisting of SEQ ID NOs: 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79 and the sequences complementary thereto. One aspect of the present invention is an isolated, purified, or enriched nucleic acid capable of hybridizing to the nucleic acid of this embodiment under conditions of high stringency. Another aspect of the present invention is an isolated, purified, or enriched nucleic acid capable of hybridizing to the nucleic acid of this embodiment under conditions of moderate stringency. Another aspect of the present invention is an isolated, purified, or enriched nucleic acid capable of hybridizing to the nucleic acid of this embodiment under conditions of low stringency. Another aspect of the present invention is an isolated, purified, or enriched nucleic acid having at least 70% homology to the nucleic acid of this embodiment as determined by analysis with BLASTN version 2.0 with the default parameters. Another aspect of the present invention is an isolated, purified, or enriched nucleic acid having at least 99% homology to the nucleic acid of this embodiment as determined by analysis with BLASTN version 2.0 with the default parameters.

Another embodiment of the present invention is an isolated, purified, or enriched nucleic acid comprising at least 10 consecutive bases of a sequence selected from the group consisting of SEO ID NOs: 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79 and the sequences complementary thereto. One aspect of the present invention is an isolated, purified, or enriched nucleic acid having at least 70% homology to the nucleic acid of this embodiment as determined by analysis with BLASTN version 2.0 with the default parameters.

Another embodiment of the present invention is an isolated, purified, or enriched nucleic acid comprising a sequence selected from the group consisting of SEQ ID NOs: 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73, 77 and the sequences complementary thereto. One aspect of the present invention is an isolated, purified, or enriched nucleic acid capable of hybridizing to the nucleic acid of this embodiment under conditions of high stringency. Another aspect of the present invention is an isolated, purified, or enriched nucleic acid capable of hybridizing to the nucleic acid of this embodiment under conditions of moderate stringency. Another aspect of the present invention is an isolated, purified, or enriched nucleic acid capable of hybridizing to the nucleic acid of this embodiment under conditions of low stringency. Another aspect of the present invention is an isolated, purified, or enriched nucleic acid having at least 70% homology to the nucleic acid of this embodiment as determined by analysis

with BLASTN version 2.0 with the default parameters. Another aspect of the present invention is an isolated, purified, or enriched nucleic acid having at least 99% homology to the nucleic acid of this embodiment as determined by analysis with BLASTN version 2.0 with the default parameters.

Another embodiment of the present invention is an isolated, purified, or enriched nucleic acid comprising at least 10 consecutive bases of a sequence selected from the group consisting of SEQ ID NOs: 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73, 77 and the sequences complementary thereto. One aspect of the present invention is an isolated, purified, or enriched nucleic acid having at least 70% homology to the nucleic acid of this embodiment as determined by analysis with BLASTN version 2.0 with the default parameters. Another aspect of the present invention is an isolated, purified, or enriched nucleic acid having at least 99% homology to the nucleic acid of this embodiment as determined by analysis with BLASTN version 2.0 with the default parameters.

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Another embodiment of the present invention is an isolated, purified, or enriched nucleic acid encoding a polypeptide having a sequence selected from the group consisting of SEO ID NOs: 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, and 80.

Another embodiment of the present invention is an isolated, purified, or enriched nucleic acid encoding a polypeptide comprising at least 10 consecutive amino acids of a polypeptide having a sequence selected from the group consisting of SEO ID NOs: 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, and 80.

Another embodiment of the present invention is an isolated, purified, or enriched nucleic acid encoding a polypeptide having a sequence selected from the group consisting of SEO ID NOs: 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78.

Another embodiment of the present invention is an isolated, purified, or enriched nucleic acid encoding a polypeptide comprising at least 10 consecutive amino acids of a polypeptide having a sequence selected from the group consisting of SEQ ID NOs: 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78.

Another embodiment of the present invention is an isolated or purified polypeptide comprising a sequence selected from the group consisting of SEQ ID NOs: 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, and 80. Another aspect of the present invention is an isolated or purified polypeptide comprising at least 10 consecutive amino acids of the polypeptides of this embodiment. Another aspect of the present invention is an isolated or purified polypeptide having at least 70% homology to the polypeptide of this embodiment as determined by analysis with FASTA version 3.0178 with the default parameters. Another aspect of the present invention is an isolated or purified polypeptide having at least 99% homology to the polypeptide of this embodiment as determined by analysis with FASTA version 3.0178 with the default parameters. Another aspect of the present invention is an isolated or purified polypeptide having at least 70% homology to an isolated or purified polypeptide comprising at least 10 consecutive amino acids of the polypeptides of this embodiment as determined by analysis with FASTA version 3.0178 with the default parameters. Another aspect of the present invention is an isolated or purified polypeptide comprising at least 10 having at least 99% homology to the polypeptide of to an isolated or purified polypeptide comprising at least 10

consecutive amino acids of the polypeptides of this embodiment as determined by analysis with FASTA version 3.0t78 with the default parameters.

Another aspect of the present invention is an isolated or purified polypeptide comprising a sequence selected from the group consisting of SEQ ID NOs: 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78. One aspect of the present invention is an isolated or purified polypeptide comprising at least 10 consecutive amino acids of the polypeptides of this embodiment. Another aspect of the present invention is an isolated or purified polypeptide having at least 70% homology to the polypeptides of this embodiment as determined by analysis with FASTA version 3.0t78 with the default parameters. Another aspect of the present invention is an isolated or purified polypeptide having at least 99% homology to the polypeptides of this embodiment as determined by analysis with FASTA version 3.0t78 with the default parameters. Another aspect of the present invention is An isolated or purified polypeptide having at least 70% homology to an isolated or purified polypeptide comprising at least 10 consecutive amino acids of the polypeptides of this embodiment as determined by analysis with FASTA version 3.0t78 with the default parameters. Another aspect of the present invention is an isolated or purified polypeptide having at least 99% homology to an isolated or purified polypeptide comprising at least 10 consecutive amino acids of the polypeptides of this embodiment as determined by analysis with FASTA version 3.0t78 with the default parameters.

Another embodiment of the present invention is an isolated or purified antibody capable of specifically binding to a polypeptide comprising a sequence selected from the group consisting of SEQ ID NOs: 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, and 80.

Another embodiment of the present invention is an isolated or purified antibody capable of specifically binding to a polypeptide comprising at least 10 consecutive amino acids of one of the polypeptides of SEO ID NOs: 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, and 80.

Another embodiment of the present invention is an isolated or purified antibody capable of specifically binding to a polypeptide having a sequence selected from the group consisting of SEO ID NOs: 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78.

Another embodiment of the present invention is an isolated or purified antibody capable of specifically binding to a polypeptide comprising at least 10 consecutive amino acids of one of the polypeptides of SEQ ID NOs: 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78.

Another embodiment of the present invention is a method of making a polypeptide having a sequence selected from the group consisting of SEQ ID NOs: 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, and 80 comprising introducing a nucleic acid encoding said polypeptide, said nucleic acid being operably linked to a promoter, into a host cell.

Another embodiment of the present invention is a method of making a polypeptide comprising at least 10 amino acids of a sequence selected from the group consisting of the sequences of SEQ ID NOs: 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, and 80 comprising introducing a nucleic acid encoding said polypeptide, said nucleic acid being operably linked to a promoter, into a host cell.

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Another embodiment of the present invention is a method of making a polypeptide having a sequence selected from the group consisting of SEQ ID NOs: 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78 comprising introducing a nucleic acid encoding said polypeptide, said nucleic acid being operably linked to a promoter, into a host cell.

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Another embodiment of the present invention is a method of making a polypeptide comprising at least 10 amino acids of a sequence selected from the group consisting of the sequences of SEQ ID NOs: 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78 comprising introducing a nucleic acid encoding said polypeptide, said nucleic acid being operably linked to a promoter, into a host cell.

Another embodiment of the present i method of generating a variant comprising obtaining a nucleic acid

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comprising a sequence selected from the group consisting of SEQ ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77, the sequences complementary to the sequences of SEQ ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77, fragments comprising at least 30 consecutive nucleotides of SEQ ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77, and fragments comprising at least 30 consecutive nucleotides of the sequences complementary to SEQ ID NOS. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 and changing one or more nucleotides in said sequence to another nucleotide, deleting

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of said variant.

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Another embodiment of the present invention is a computer readable medium having stored thereon a sequence selected from the group consisting of a nucleic acid code of SEOID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 and a polypeptide code of SEO ID NOs. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78.

one or more nucleotides in said sequence, or adding one or more nucleotides to said sequence. In one aspect of the present invention, the method further comprises the step of testing the enzymatic properties of a translation product

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Another embodiment of the present invention is a computer system comprising a processor and a data storage device wherein said data storage device has stored thereon a sequence selected from the group consisting of a nucleic acid code of SEQID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 and a polypeptide code of SEQID NOs. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78. In one aspect of the present invention, the computer system further comprises a sequence comparer and a data storage device having reference sequences stored thereon. For example, the sequence comparer may comprise a computer program which indicates polymorphisms. In another aspect of the present invention is the computer system of this embodiment further comprises an identifier which identifies features in said sequence.

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Another embodiment of the present invention is a method for comparing a first sequence to a reference sequence wherein said first sequence is selected from the group consisting of a nucleic acid code of SEQID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 and a polypeptide code of SEQ ID NOs. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 68, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78 comprising the steps of reading said first sequence and said reference sequence through use of a computer program which compares sequences; and determining differences between said first sequence and said reference sequence with said computer program. In one aspect of the present invention, the step of determining differences between the first sequence and the reference sequence comprises identifying polymorphisms.

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Another embodiment of the present invention is a method for identifying a feature in a sequence selected from the group consisting of a nucleic acid code of SEQID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 and a polypeptide code of SEQ ID NOs. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78 comprising the steps of reading said sequence through the use of a computer program which identifies features in sequences and identifying features in said sequence with said computer program.

Brief Description of the Drawings

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Figure 1 shows the locations of coding regions, the %G-C. and the %DNA identity between the approximately 28Kb of common sequence in fosmids 101G10 and 60A5.

Figure 2 shows the sequences surrounding the TATA boxes of several promoters from *Cenarchaeum* symbiosum and the distances from the TATA boxes to the initiation codons in these sequences.

Figure 3 is a block diagram of an exemplary computer system.

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Figure 4 is a flow diagram illustrating one embodiment of a process 200 for comparing a new nucleotide or protein sequence with a database of sequences in order to determine the homology levels between the new sequence and the sequences in the database.

Figure 5 is a flow diagram illustrating one embodiment of a process 250 in a computer for determining whether two sequences are homologous.

Figure 6 is a flow diagram illustrating one embodiment of an identifier process for detecting the presence of a feature in a sequence.

Definitions

The term "gene" means the segment of DNA involved in producing a polypeptide chain; it includes regions preceding and following the coding region (leader and trailer) as well as, where applicable, intervening sequences (introns) between individual coding segments (exons).

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As used herein, the term "isolated" means that the material is removed from its original environment (e.g.,

the natural environment if it is naturally occurring). For example, a naturally-occurring polynucleotide or polypeptide present in a living animal is not isolated, but the same polynucleotide or polypeptide, separated from some or all of the coexisting materials in the natural system, is isolated. Such polynucleotides could be part of a vector and/or such polynucleotides or polypeptides could be part of a composition, and still be isolated in that such vector or composition is not part of its natural environment.

As used herein, the term "purified" does not require absolute purity; rather, it is intended as a relative definition. Individual nucleic acids obtained from a library have been conventionally purified to electrophoretic homogeneity. The sequences obtained from these clones could not be obtained directly either from the library or from total human DNA. The purified nucleic acids of the present invention have been purified from the remainder of the genomic DNA in the organism by at least 10⁴-10⁶ fold. However, the term "purified" also includes nucleic acids which have been purified from the remainder of the genomic DNA or from other sequences in a library or other environment by at least one order of magnitude, preferably two or three orders, and more preferably four or five orders of magnitude.

As used herein, the term "recombinant" means that the nucleic acid is adjacent to "backbone" nucleic acid to which it is not adjacent in its natural environment. Additionally, to be "enriched" the nucleic acids will represent 5% or more of the number of nucleic acid inserts in a population of nucleic acid backbone molecules. Backbone molecules according to the present invention include nucleic acids such as expression vectors, self-replicating nucleic acids, viruses, integrating nucleic acids, and other vectors or nucleic acids used to maintain or manipulate a nucleic acid insert of interest. Preferably, the enriched nucleic acids represent 15% or more of the number of nucleic acid inserts in the population of recombinant backbone molecules. More preferably, the enriched nucleic acids represent 50% or more of the number of nucleic acid inserts in the population of recombinant backbone molecules. In a highly preferred embodiment, the enriched nucleic acids represent 90% or more of the number of nucleic acid inserts in the population of recombinant backbone molecules.

A promoter sequence is "operably linked to" a coding sequence when RNA polymerase which initiates transcription at the promoter will transcribe the coding sequence into mRNA.

"Recombinant" polypeptides or proteins refer to polypeptides or proteins produced by recombinant DNA techniques; i.e., produced from cells transformed by an exogenous DNA construct encoding the desired polypeptide or protein. "Synthetic" polypeptides or protein are those prepared by chemical synthesis.

A DNA "coding sequence" or a "nucleotide sequence encoding" a particular polypeptide or protein, is a DNA sequence which is transcribed and translated into a polypeptide or protein when placed under the control of appropriate regulatory sequences.

"Plasmids" are designated by a lower case p preceded and/or followed by capital letters and/or numbers. The starting plasmids herein are either commercially available, publicly available on an unrestricted basis, or can be constructed from available plasmids in accord with published procedures. In addition, equivalent plasmids to those described herein are known in the art and will be apparent to the ordinarily skilled artisan.

"Digestion" of DNA refers to catalytic cleavage of the DNA with a restriction enzyme that acts only at

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certain sequences in the DNA. The various restriction enzymes used herein are commercially available and their reaction conditions, cofactors and other requirements were used as would be known to the ordinarily skilled artisan. For analytical purposes, typically 1 g of plasmid or DNA fragment is used with about 2 units of enzyme in about 20 l of buffer solution. For the purpose of isolating DNA fragments for plasmid construction, typically 5 to 50 g of DNA are digested with 20 to 250 units of enzyme in a larger volume. Appropriate buffers and substrate amounts for particular restriction enzymes are specified by the manufacturer. Incubation times of about 1 hour at 37 C are ordinarily used, but may vary in accordance with the supplier's instructions. After digestion the gel electrophoresis may be performed to isolate the desired fragment.

"Oligonucleotide" refers to either a single stranded polydeoxynucleotide or two complementary polydeoxynucleotide strands which may be chemically synthesized. Such synthetic oligonucleotides have no 5' phosphate and thus will not ligate to another oligonucleotide without adding a phosphate with an ATP in the presence of a kinase. A synthetic oligonucleotide will ligate to a fragment that has not been dephosphorylated.

Detailed Description of the Preferred Embodiment

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In order to begin the characterization of *Cenarchaeum symbiosum*, a large region of the *C. symbiosum* genome was sequenced. In particular, two overlapping *C. symbiosum*-derived fosmid inserts of approximately 42kb and 33kb were sequenced. The sequences of the two fosmid inserts revealed that there are at least two major variants or strains of *C. symbiosum* that coexist inside the sponge tissues of a single sponge. This complexity of the *C. symbiosum* population was not detected in initial studies based solely on direct sequencing of PCR amplified SSU genes. (Preston, C. M. *et al.* 1996. A psychrophilic crenarchaeon inhabits a marine sponge: Cenarchaeum symbiosum gen. nov., sp. nov. *Proc. Natl. Acad. Sci.* USA 93, 6241-6246) This natural variation would also have been lost upon isolation of a pure culture.

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The Cenarchaeum symbiosum sequences obtained from the two fosmids containing overlapping genomic inserts are provided in the accompanying sequence listing and are identified as SEO ID NO: 1 and SEO ID NO: 2. The two fosmid sequences were not entirely identical in their overlapping portions but instead contained differences. Upon further investigation, it was discovered that the two fosmid sequences were derived from two different, but closely related, strains of Cenarchaeum symbiosum (called variant A and variant B) which may simultaneously inhabit a single sponge.

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Within the sequences of the fosmid inserts, numerous open reading frames encoding polypeptides having homology to known proteins, as well as open reading frames encoding proteins which do not exhibit homology to known proteins, were identified. Homology was determined using the program FASTA with the default parameters. The polypeptides encoded by these sequences are identified in the accompanying sequence listing as SEQ ID NOs: 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76 and 80 (polypeptides with homology to known proteins) and SEQ ID NOs: 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74 and 78 (polypeptides

without homology to known proteins). In addition, sequences encoding the 16S rRNA, the 23S rRNA and a tyrosine tRNAs were also identified.

One aspect of the present invention is an isolated, purified, or enriched nucleic acid comprising one of the sequences of SEQ ID NOs: 1, 2, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77 and 79 the sequences complementary thereto, or a fragment comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive bases of one of the sequences of SEQ ID NOs: 1, 2, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77 and 79 or the sequences complementary thereto. The isolated, purified or enriched nucleic acids may comprise DNA, including cDNA, genomic DNA, and synthetic DNA. The DNA may be double-stranded or single-stranded, and if single stranded may be the coding strand or non-coding (anti-sense) strand. Alternatively, the isolated, purified or enriched nucleic acids may comprise RNA.

As discussed in more detail below, the isolated, purified, or enriched nucleic acids of one of SEO ID NOs: 1, 2, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77 and 79 may be used to prepare one of the polypeptides of SEO ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, and 80 or fragments comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids of one of the polypeptides of SEO ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, and 80.

Accordingly, another aspect of the present invention is an isolated, purified, or enriched nucleic acid which encodes one of the polypeptides of SEO ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74 76, 78, and 80 or fragments comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids of one of the polypeptides of SEO ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74 76, 78, and 80. The coding sequences of these nucleic acids may be identical to one of the coding sequences of one of the nucleic acids of SEO ID NOs: 1, 2, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77 and 79 or a fragment thereof or may be different coding sequences which encode one of the polypeptides of SEO ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74 76, 78, and 80 or fragments comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids of one of the polypeptides of SEO ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74 76, 78, and 80 or fragments comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids of one of the polypeptides of SEO ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74 76, 78, and 80 as a result of the redundancy or degeneracy of the genetic code. The genetic code is well known to those of skill in the art and can be obtained, for example, on page 214 of B. Lewin, Genes VI, Oxford University Press, 1997.

The isolated, purified, or enriched nucleic acid which encodes one of the polypeptides of SEO ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68,

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70, 72, 74 76, 78, and 80 may include, but is not limited to: only the coding sequence of one of SEQ ID NOs: 1, 2, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77 and 79; the coding sequences of SEQ ID NOs: 1, 2, 3, 5, 7, 8, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77 and 79 and additional coding sequences, such as leader sequences or proprotein sequences; or the coding sequences of SEQ ID NOs: 1, 2, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77 and 79 and non-coding sequences, such as introns or non-coding sequences 5' and/or 3' of the coding sequence. Thus, as used herein, the term "polynucleotide encoding a polynucleotide which includes only coding sequence for the polypeptide as well as a polynucleotide which includes additional coding and/or non-coding sequence.

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Alternatively, the nucleic acid sequences of SEO ID NOs: 1, 2, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77 and 79 may be mutagenized using conventional techniques, such as site directed mutagenesis, or other techniques familiar to those skilled in the art, to introduce silent changes into the polynucleotides of SEO ID NOs: 1, 2, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77 and 79. As used herein, "silent changes" include, for example, changes which do not alter the amino acid sequence encoded by the polynucleotide. Such changes may be desirable in order to increase the level of the polypeptide produced by host cells containing a vector encoding the polypeptide by introducing codons or codon pairs which occur frequently in the host organism.

The present invention also relates to polynucleotides which have nucleotide changes which result in amino

acid substitutions, additions, deletions, fusions and truncations in the polypeptides of SEO ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, and 80. Such nucleotide changes may be introduced using techniques such as site directed mutagenesis, random chemical mutagenesis, exonuclease III deletion, and other recombinant DNA techniques. Alternatively, such nucleotide changes may be naturally occurring allelic variants which are isolated by identifying nucleic acids which specifically hybridize to probes comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive bases of one of the sequences of SEO ID NOs: 1, 2, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77 and 79 or the sequences complementary thereto to nucleic acids from *Cenarchaeum symbiosum* or related organisms under

The isolated, purified, or enriched nucleic acids of SEO ID NOs: 1, 2, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77 and 79, the sequences complementary thereto, or a fragment comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive bases of one of the sequences of SEO ID NOs: 1, 2, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77

conditions of high, moderate, or low strigency as provided herein.

and 79 or the sequences complementary thereto may also be used as probes to identify the presence of *Cenarchaeum symbiosum* in a biological sample. In such procedures, a biological sample potentially harboring *Cenarchaeum symbiosum* is obtained and nucleic acids are obtained from the sample. The nucleic acids are contacted with the probe under conditions which permit the probe to specifically hybridize to any complementary sequences from *Cenarchaeum symbiosum* which are present therein.

Where necessary, conditions which permit the probe to specifically hybridize to complementary sequences from *Cenarchaeum symbiosum* may be determined by placing the probe in contact with complementary sequences from *Cenarchaeum symbiosum* as well as control sequences which are not from *Cenarchaeum symbiosum*. In some analyses, the control sequences may be from organisms related to *Cenarchaeum symbiosum*. Alternatively, the control sequences may be from organisms which are not related to *Cenarchaeum symbiosum*. Hybridization conditions, such as the salt concentration of the hybridization buffer, the formamide concentration of the hybridization buffer, or the hybridization temperature, may be varied to identify conditions which allow the probe to hybridize specifically to nucleic acids from *Cenarchaeum symbiosum*.

If the sample contains nucleic acids from *Cenarchaeum symbiosum*, specific hybridization of the probe to the nucleic acids from *Cenarchaeum symbiosum* is then detected. Hybridization may be detected by labeling the probe with a detectable agent such as a radioactive isotope, a fluorescent dye or an enzyme capable of catalyzing the formation of a detectable product.

Many methods for using the labeled probes to detect the presence of nucleic acids from *Cenarchaeum symbiosum* in a sample are familiar to those skilled in the art. These include Southern Blots, Northern Blots, colony hybridization procedures, and dot blots. Protocols for each of these procedures are provided in Ausubel et al. Current Protocols in Molecular Biology, John Wiley 503 Sons, Inc. 1997 and Sambrook et al., Molecular Cloning: A Laboratory Manual 2d Ed., Cold Spring Harbor Laboratory Press, 1989.

Alternatively, more than one probe (at least one of which is capable of specifically hybridizing to any complementary sequences from *Cenarchaeum symbiosum* which are present in the nucleic acid sample), may be used in an amplification reaction to determine whether the nucleic acid sample contains nucleic acids from *Cenarchaeum symbiosum*. Preferably, the probes comprise oligonucleotides. In one embodiment, the amplification reaction may comprise a PCR reaction. PCR protocols are described in Ausubel and Sambrook, *supra*. Alternatively, the amplification may comprise a ligase chain reaction, 3SR, or strend displacement reaction. (See Barany, F., "The Ligase Chain Reaction in a PCR World", *PCR Methods and Applications* 1:5-16 (1991); E. Fahy *et al.*, "Self-sustained Sequence Replication (3SR): An Isothermal Transcription-based Amplification System Alternative to PCR", *PCR Methods and Applications* 1:25-33 (1991); and Walker G.T. *et al.*, "Strand Displacement Amplification-an Isothermal *in vitro* DNA Amplification Technique, *Nucleic Acid Research* 20:1691-1696 (1992). In such procedures, the nucleic acids in the sample are contacted with the probes, the amplification reaction is performed, and any resulting amplification product is detected. The amplification product may be detected by performing gel electrophoresis on the reaction products and staining the gel with an interculator such as ethicium bromide. Alternatively, one or more of the probes may be labeled with a radioactive

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isotope and the presence of a radioactive amplification product may be detected by autoradiography after gel electrophoresis.

Probes derived from sequences near the ends of the sequences of SEQ ID Nos: 1 and 2 may also be used in chromosome walking procedures to identify clones containing genomic sequences located adjacent to the sequences of SEQ ID Nos: 1 and 2. Such methods allow the isolation of genes which encode additional proteins expressed in Cenarchaeum symbiosum and facilitate the further physiological characterization of the organism.

Another aspect of the present invention is a method for determining whether a sample contains variant A and/or variant B of Cenarchaeum symbiosum. In such procedures, a sample potentially harboring variant A and/or variant B Cenarchaeum symbiosum is obtained and nucleic acids are obtained from the sample. The nucleic acids are contacted with the probe under conditions which permit the probe to specifically hybridize to any complementary sequences from variant A or variant B of Cenarchaeum symbiosum which are present therein. Preferably, the probe comprises a sequence having one or more nucleotides which differ between variant A and variant B. Conditions in which the probe specifically hybridizes to nucleic acids from one of the variants but not to nucleic acids from the other variant may be determined by contacting the probe with its corresponding sequence from variant A and variant B and varying the hybridization conditions, such as the salt concentration of the hybridization buffer, the formamide concentration of the buffer, or the hybridization temperature, to identify conditions in which the probe hybridizes to the corresponding sequence from one variant but not to the corresponding sequence from the other variant. Hybridization of the probe to nucleic acids from the Cenarchaeum symbiosum variant is then detected using any of the procedures described above.

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The isolated, purified, or enriched nucleic acids of SEQ ID NOs: 1, 2, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77 and 79, the sequences complementary thereto, or a fragment comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive bases of one of the sequences of SEQ ID NOs: 1, 2, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77 and 79 or the sequences complementary thereto may be used as probes to identify and isolate cDNAs encoding the polypeptides of SEO ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50. 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74 76, 78, and 80. In such procedures, a cDNA library is constructed from a sample containing Cenarchaeum symbiosum. The cDNA library is then contacted with a probe comprising a coding sequence, or a fragment of a coding sequence, encoding one of the polypeptides of SEQ ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74 76, 78, and 80 or a fragment thereof under conditions which permit the probe to specifically hybridize to sequences complementary thereto. cDNAs which hybridize to the probe are then detected and isolated. Procedures for preparing and identifying cDNAs are disclosed in Ausubel et al. Current Protocols in Molecular Biology, John Wiley 503 Sons, Inc. 1997 and Sambrook et al., Molecular Cloning: A Laboratory Manual 2d Ed., Cold Spring Harbor Laboratory Press, 1989.

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The isolated, purified, or enriched nucleic acids of SEQ ID NOs: 1, 2, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77 and 79, the sequences complementary thereto, or a fragment comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive bases of one of the sequences of SEQ ID NOs: 1, 2, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77 and 79 or the sequences complementary thereto may be used as probes to identify and isolate related nucleic acids. In some embodiments, the related nucleic acids may be cDNAs or genomic DNAs from organisms other than *Cenarchaeum symbiosum*. For example, the other organisms may be organisms which are related to *Cenarchaeum symbiosum*. In such procedures, a nucleic acid sample containing nucleic acids from the related organism, such as a cDNA or genomic DNA library from the related organism, is contacted with the probe under conditions which permit the probe to specifically hybridize to related sequences. Hybridization of the probe to nucleic acids from the related organism is then detected using any of the methods described above.

Hybridization may be carried out under conditions of low stringency, moderate stringency or high stringency. As an example of nucleic acid hybridization, a polymer membrane containing immobilized denatured nucleic acids is first prehybridized for 30 minutes at 45 C in a solution consisting of 0.9 M NaCl, 50 mM NaH₂PO₄, pH 7.0, 5.0 mM Na₂EDTA, 0.5% SDS, 10X Denhardt's, and 0.5 mg/ml polyriboadenylic acid. Approximately 2 X 10⁷ cpm (specific activity 4-9 X 10⁸ cpm/ug) of ³²P end-labeled oligonucleotide probe are then added to the solution. After 12-16 hours of incubation, the membrane is washed for 30 minutes at room temperature in 1X SET (150 mM NaCl, 20 mM Tris hydrochloride, pH 7.8, 1 mM Na₂EDTA) containing 0.5% SDS, followed by a 30 minute wash in fresh 1X SET at Tm-10 C for the oligonucleotide probe. The membrane is then exposed to auto-radiographic film for detection of hybridization signals.

By varying the stringency of the hybridization conditions used to identify nucleic acids, such as cDNAs or genomic DNAs, which hybridize to the detectable probe, nucleic acids having different levels of homology to the probe can be identified and isolated. Stringency may be varied by conducting the hybridization at varying temperatures below the melting temperatures of the probes. The melting temperature of the probe may be calculated using the following formulas:

For probes between 14 and 70 nucleotides in length the melting temperature (Tm) is calculated using the formula: Tm = 81.5 + 16.6(log [Na+]) + 0.41(fraction G+C)-(600/N) where N is the length of the probe.

If the hybridization is carried out in a solution containing formamide, the melting temperature may be calculated using the equation Tm=81.5+16.6(log [Na+])+0.41(fraction G+C)-(0.63% formamide)-(600/N) where N is the length of the probe.

Prehybridization may be carried out in 6X SSC, 5X Denhardt's reagent, 0.5% SDS, 100 g denatured fragmented salmon sperm DNA or 6X SSC, 5X Denhardt's reagent, 0.5% SDS, 100 g denatured fragmented salmon sperm DNA, 50% formamide. The formulas for SSC and Denhardt's solutions are listed in Sambrook et al., *supra*.

Hybridization is conducted by adding the detectable probe to the prehybridization solutions listed above. Where the probe comprises double stranded DNA, it is denatured before addition to the hybridization solution. The filter is

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contacted with the hybridization solution for a sufficient period of time to allow the probe to hybridize to cDNAs or genomic DNAs containing sequences complementary thereto or homologous thereto. For probes over 200 nucleotides in length, the hybridization may be carried out at 15-25 C below the Tm. For shorter probes, such as oligonucleotide probes, the hybridization may be conducted at 5-10 C below the Tm. Preferably, for hybridizations in 6X SSC, the hybridization is conducted at approximately 68 C. Preferably, for hybridizations in 50% formamide containing solutions, the hybridization is conducted at approximately 42 C.

All of the foregoing hybridizations would be considered to be under conditions of high stringency.

Following hybridization, the filter is washed in 2X SSC, 0.1% SDS at room temperature for 15 minutes. The filter is then washed with 0.1X SSC, 0.5% SDS at room temperature for 30 minutes to 1 hour. Thereafter, the solution is washed at the hybridization temperature in 0.1X SSC, 0.5% SDS. A final wash is conducted in 0.1X SSC at room temperature.

Nucleic acids which have hybridized to the probe are identified by autoradiography or other conventional techniques.

The above procedure may be modified to identify nucleic acids having decreasing levels of homology to the probe sequence. For example, to obtain nucleic acids of decreasing homology to the detectable probe, less stringent conditions may be used. For example, the hybridization temperature may be decreased in increments of 5 C from 68 C to 42 C in a hybridization buffer having a Na+ concentration of approximately 1M. Following hybridization, the filter may be washed with 2X SSC, 0.5% SDS at the temperature of hybridization. These conditions are considered to be "moderate" conditions above 50 C and "low" conditions below 50 C. A specific example of "moderate" hybridization conditions is when the above hybridization is conducted at 55 C. A specific example of "low stringency" hybridization conditions is when the above hybridization is conducted at 45 C.

Alternatively, the hybridization may be carried out in buffers, such as 6X SSC, containing formamide at a temperature of 42 C. In this case, the concentration of formamide in the hybridization buffer may be reduced in 5% increments from 50% to 0% to identify clones having decreasing levels of homology to the probe. Following hybridization, the filter may be washed with 6X SSC, 0.5% SDS at 50 C. These conditions are considered to be "moderate" conditions above 25% formamide and "low" conditions below 25% formamide. A specific example of "moderate" hybridization conditions is when the above hybridization is conducted at 30% formamide. A specific example of "low stringency" hybridization conditions is when the above hybridization is conducted at 10% formamide.

Nucleic acids which have hybridized to the probe are identified by autoradiography.

For example, the preceding methods may be used to isolate nucleic acids having a sequence with at least 97%, at least 95%, at least 85%, at least 80%, or at least 70% homology to a nucleic acid sequence selected from the group consisting of one of the sequences of SEO ID NOS. 1, 2, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77 and 79, fragments comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive bases thereof, and the sequences complementary thereto. Homology may be measured using BLASTN version 2.0

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with the default parameters. For example, the homologous polynucleotides may have a coding sequence which is a naturally occurring allelic variant of one of the coding sequences described herein. Such allelic variants may have a substitution, deletion or addition of one or more nucleotides when compared to the nucleic acids of SEQ ID NOs: 1, 2, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77 and 79 or the sequences complementary thereto.

Additionally, the above procedures may be used to isolate nucleic acids which encode polypeptides having at

least 99%, 95%, at least 90%, at least 85%, at least 80%, or at least 70% homology to a polypeptide having the sequence of one of SEQ ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74 76, 78, and 80 or fragments comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids thereof as determined using the FASTA version 3.0t78

algorithm with the default parameters.

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Another aspect of the present invention is an isolated or purified polypeptide comprising the sequence of one of SEO ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74 76, 78, and 80 or fragments comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids thereof. As discussed above, such polypeptides may be obtained by inserting a nucleic acid encoding the polypeptide into a vector such that the coding sequence is operably linked to a sequence capable of driving the expression of the encoded polypeptide in a suitable host cell. For example, the expression vector may comprise a promoter, a ribosome binding site for translation initiation and a transcription terminator. The vector may also include appropriate sequences for amplifying expression.

Promoters suitable for expressing the polypeptide or fragment thereof in bacteria include the $\underline{E.~coli.~lac}$ or \underline{trp} promoters, the lacl promoter, the lacZ promoter, the T3 promoter, the T7 promoter, the gpt promoter, the lambda P_R promoter, the lambda P_L promoter the trp promoter, promoters from operons encoding glycolytic enzymes such as 3-phosphoglycerate kinase (PGK), and the acid phosphatase promoter. Fungal promoters include the α factor promoter. Eukaryotic promoters include the CMV immediate early promoter, the HSV thymidine kinase promoter, heat shock promoters, the early and late SV40 promoter, LTRs from retroviruses, and the mouse metallothionein-I promoter. Other promoters known to control expression of genes in prokaryotic or eukaryotic cells or their viruses may also be used.

Mammalian expression vectors may also comprise an origin of replication, any necessary ribosome binding sites, a polyadenylation site, splice donor and acceptor sites, transcriptional termination sequences, and 5' flanking nontranscribed sequences. In some embodiments, DNA sequences derived from the SV40 splice and polyadenylation sites may be used to provide the required nontranscribed genetic elements.

Vectors for expressing the polypeptide or fragment thereof in eukaryotic cells may also contain enhancers to increase expression levels. Enhancers are cis-acting elements of DNA, usually from about 10 to about 300 bp in length that act on a promoter to increase its transcription. Examples include the SV40 enhancer on the late side of the

replication origin bp 100 to 270, the cytomegalovirus early promoter enhancer, the polyoma enhancer on the late side of the replication origin, and the adenovirus enhancers.

In addition, the expression vectors preferably contain one or more selectable marker genes to permit selection of host cells containing the vector. Such selectable markers include genes encoding dihydrofolate reductase or genes conferring neomycin resistance for eukaryotic cell culture, genes conferring tetracycline or ampicillin resistance in <u>E. coli</u>, and the <u>S. cerevisiae</u> TRP1 gene.

In some embodiments, the nucleic acid encoding one of the polypeptides of SEO ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, and 80 or fragments comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids thereof is assembled in appropriate phase with a leader sequence capable of directing secretion of the translated polypeptide or fragment thereof. Optionally, the nucleic acid can encode a fusion polypeptide in which one of the polypeptides of SEO ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, and 80 or fragments comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids thereof is fused to heterologous peptides or polypeptides, such as N-terminal identification peptides which impart desired characteristics, such as increased stability or simplified purification.

The appropriate DNA sequence may be inserted into the vector by a variety of procedures. In general, the DNA sequence is ligated to the desired position in the vector following digestion of the insert and the vector with appropriate restriction endonucleases. Alternatively, blunt ends in both the insert and the vector may be ligated. A variety of cloning techniques are disclosed in Ausubel et al. Current Protocols in Molecular Biology, John Wiley 503 Sons, Inc. 1997 and Sambrook et al., Molecular Cloning: A Laboratory Manual 2d Ed., Cold Spring Harbor Laboratory Press, 1989. Such procedures and others are deemed to be within the scope of those skilled in the art.

The vector may be, for example, in the form of a plasmid, a viral particle, or a phage. Other vectors include chromosomal, nonchromosomal and synthetic DNA sequences, derivatives of SV40; bacterial plasmids, phage DNA, baculovirus, yeast plasmids, vectors derived from combinations of plasmids and phage DNA, viral DNA such as vaccinia, adenovirus, fowl pox virus, and pseudorabies. A variety of cloning and expression vectors for use with prokaryotic and eukaryotic hosts are described by Sambrook, et al., Molecular Cloning: A Laboratory Manual, Second Edition, Cold Spring Harbor, N.Y., (1989).

Particular bacterial vectors which may be used include the commercially available plasmids comprising genetic elements of the well known cloning vector pBR322 (ATCC 37017), pKK223-3 (Pharmacia Fine Chemicals, Uppsala, Sweden), GEM1 (Promega Biotec, Madison, WI, USA) pQE70, pQE60, pQE-9 (Qiagen), pD10, psiX174 pBluescript II KS, pNH8A, pNH16a, pNH18A, pNH46A (Stratagene), ptrc99a, pKK223-3, pKK233-3, pDR540, pRIT5 (Pharmacia), pKK232-8 and pCM7. Particular eukaryotic vectors include pSV2CAT, pQG44, pXT1, pSG (Stratagene) pSVK3, pBPV, pMSG, and pSVL (Pharmacia). However, any other vector may be used as long as it is replicable and viable in the host cell.

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The host cell may be any of the host cells familiar to those skilled in the art, including prokaryotic cells, eukaryotic cells, mammalian cells, insect cells, or plant cells. As representative examples of appropriate hosts, there may be mentioned: bacterial cells, such as <u>E. coli</u>, <u>Streptomyces</u>, <u>Bacillus subtilis</u>, <u>Salmonella typhimurium</u> and various species within the genera Pseudomonas, Streptomyces, and Staphylococcus, fungal cells, such as yeast, insect cells such as <u>Drosophila S2</u> and <u>Spodoptera Sf9</u>, animal cells such as CHO, COS or Bowes melanoma, and adenoviruses. The selection of an appropriate host is within the abilities of those skilled in the art.

The vector may be introduced into the host cells using any of a variety of techniques, including transformation, transfection, transduction, viral infection, gene guns, or Ti-mediated gene transfer. Particular methods include calcium phosphate transfection, DEAE-Dextran mediated transfection, lipofection, or electroporation (Davis, L., Dibner, M., Battey, I., Basic Methods in Molecular Biology, (1986)).

Where appropriate, the engineered host cells can be cultured in conventional nutrient media modified as appropriate for activating promoters, selecting transformants or amplifying the genes of the present invention. Following transformation of a suitable host strain and growth of the host strain to an appropriate cell density, the selected promoter may be induced by appropriate means (e.g., temperature shift or chemical induction) and the cells may be cultured for an additional period to allow them to produce the desired polypeptide or fragment thereof.

Cells are typically harvested by centrifugation, disrupted by physical or chemical means, and the resulting crude extract is retained for further purification. Microbial cells employed for expression of proteins can be disrupted by any convenient method, including freeze-thaw cycling, sonication, mechanical disruption, or use of cell lysing agents. Such methods are well known to those skilled in the art. The expressed polypeptide or fragment thereof can be recovered and purified from recombinant cell cultures by methods including ammonium sulfate or ethanol precipitation, acid extraction, anion or cation exchange chromatography, phosphocellulose chromatography, hydrophobic interaction chromatography, affinity chromatography, hydroxylapatite chromatography and lectin chromatography. Protein refolding steps can be used, as necessary, in completing configuration of the polypeptide. If desired, high performance liquid chromatography (HPLC) can be employed for final purification steps.

Various mammalian cell culture systems can also be employed to express recombinant protein. Examples of mammalian expression systems include the COS-7 lines of monkey kidney fibroblasts (described by Gluzman, Cell, 23:175 (1981), and other cell lines capable of expressing proteins from a compatible vector, such as the C127, 3T3, CHO, HeLa and BHK cell lines.

The constructs in host cells can be used in a conventional manner to produce the gene product encoded by the recombinant sequence. Depending upon the host employed in a recombinant production procedure, the polypeptides produced by host cells containing the vector may be glycosylated or may be non-glycosylated. Polypeptides of the invention may or may not also include an initial methionine amino acid residue.

Alternatively, the polypeptides of SEQ ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74 76, 78, and 80 or fragments comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids thereof can be synthetically produced

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by conventional peptide synthesizers. In other embodiments, fragments or portions of the polypeptides may be employed for producing the corresponding full-length polypeptide by peptide synthesis; therefore, the fragments may be employed as intermediates for producing the full-length polypeptides.

Cell-free translation systems can also be employed to produce one of the polypeptides of SEO ID Nos: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74 76, 78, and 80 or fragments comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids thereof using mRNAs transcribed from a DNA construct comprising a promoter operably linked to a nucleic acid encoding the polypeptide or fragment thereof. In some embodiments, the DNA construct may be linearized prior to conducting an *in vitro* transcription reaction. The transcribed mRNA is then incubated with an appropriate cell-free translation extract, such as a rabbit reticulocyte extract, to produce the desired polypeptide or fragment thereof.

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The present invention also relates to variants of the polypeptides of SEQ ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, and 80 or fragments comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids thereof. The term "variant" includes derivatives or analogs of these polypeptides. In particular, the variants may differ in amino acid sequence from the polypeptides of SEQ ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, and 80 by one or more substitutions, additions, deletions, fusions and truncations, which may be present in any combination.

The variants may be naturally occurring or created in vitro. In particular, such variants may be created using genetic engineering techniques such as site directed mutagenesis, random chemical mutagenesis, Exonuclease III deletion procedures, and standard cloning techniques. Alternatively, such variants, fragments, analogs, or derivatives may be created using chemical synthesis or modification procedures.

Other methods of making variants are also familiar to those skilled in the art. These include procedures in which nucleic acid sequences obtained from natural isolates are modified to generate nucleic acids which encode polypeptides having characteristics which enhance their value in industrial or laboratory applications. In such procedures, a large number of variant sequences having one or more nucleotide differences with respect to the sequence obtained from the natural isolate are generated and characterized. Preferably, these nucleotide differences result in amino acid changes with respect to the polypeptides encoded by the nucleic acids from the natural isolates.

For example, variants may be created using error prone PCR. In error prone PCR, PCR is performed under conditions where the copying fidelity of the DNA polymerase is low, such that a high rate of point mutations is obtained along the entire length of the PCR product. Error prone PCR is described in Leung, D.W., et al., Technique, 1:11-15 (19 89) and Caldwell, R. C. & Joyce G.F., PCR Methods Applic., 2:28-33 (1992). Briefly, in such procedures, nucleic acids to be mutagenized are mixed with PCR primers, reaction buffer, MgCl₂, MnCl₂, Taq polymerase and an appropriate concentration of dNTPs for achieving a high rate of point mutation along the entire length of the PCR product. For example, the reaction may be performed using 20 fmoles of nucleic acid to be mutagenized, 30pmole of

each PCR primer, a reaction buffer comprising 50mM KCI, 10mM Tris HCI (pH 8.3) and 0.01% gelatin, 7mM MgCl₂, 0.5mM MnCl₂, 5 units of Taq polymerase, 0.2mM dGTP, 0.2mM dATP, 1mM dCTP, and 1mM dTTP. PCR may be performed for 30 cycles of 94° C for 1 min, 45° C for 1 min, and 72° C for 1 min. However, it will be appreciated that these parameters may be varied as appropriate. The mutagenized nucleic acids are cloned into an appropriate vector and the activities of the polypeptides encoded by the mutagenized nucleic acids is evaluated.

Variants may also be created using oligonucleotide directed mutagenesis to generate site-specific mutations in any cloned DNA segment of interest. Oligonucleotide mutagenesis is described in Reidhaar-Olson, J.F. & Sauer, R.T., et al., Science, 241:53-57 (1988). Briefly, in such procedures a plurality of double stranded oligonucleotides bearing one or more mutations to be introduced into the cloned DNA are synthesized and inserted into the cloned DNA to be mutagenized. Clones containing the mutagenized DNA are recovered and the activities of the polypeptides they encode are assessed.

Another method for generating variants is assembly PCR. Assembly PCR involves the assembly of a PCR product from a mixture of small DNA fragments. A large number of different PCR reactions occur in parallel in the same vial, with the products of one reaction priming the products of another reaction. Assembly PCR is described in U.S. Patent Application Serial No. 08/677,112, filed July 9, 1997 and U.S. Patent Application Serial No. 08/942,504, filed October 31, 1997.

Still another method of genrating variants is sexual PCR mutagenesis. In sexual PCR mutagenesis, forced homologous recombination occurs between DNA molecules of different but highly related DNA sequence in vitro, as a result of random fragmentation of the DNA molecule based on sequence homology, followed by fixation of the crossover by primer extension in a PCR reaction. Sexual PCR mutagenesis is described in Stemmer, W.P., PNAS, USA, 91:10747-10751 (1994). Briefly, in such procedures a plurality of nucleic acids to be recombined are digested with DNAse to generate fragments having an average size of 50-200 nucleotides. Fragments of the desired average size are purified and resuspended in a PCR mixture. PCR is conducted under conditions which facilitate recombination between the nucleic acid fragments. For example, PCR may be performed by resuspending the purified fragments at a concentration of 10-30ng/µl in a solution of 0.2mM of each dNTP, 2.2mM MgCl2, 50mM KCL, 10mM Tris HCl, pH 9.0, and 0.1% Triton X-100. 2.5 units of Taq polymerase per 100µl of reaction mixture is added and PCR is performed using the following regime: 94° C for 60 seconds, 94° C for 30 seconds, 50-55° C for 30 seconds, 72° C for 30 seconds (30-45 times) and 72° C for 5 minutes. However, it will be appreciated that these parameters may be varied as appropriate. In some embodiments, oligonucleotides may be included in the PCR reactions. In other embodiments, the Klenow fragment of DNA polymerase I may be used in a first set of PCR reactions and Tag polymerase may be used in a subsequent set of PCR reactions. Recombinant sequences are isolated and the activities of the polypeptides they encode are assessed.

Variants may also be created by in vivo mutagenesis. In some embodiments, random mutations in a sequence of interest are generated by propagating the sequence of interest in a bacterial strain, such as an E. coli strain, which carries mutations in one or more of the DNA repair pathways. Such "mutator" strains have a higher

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random mutation rate than that of a wild-type parent. Propagating the DNA in one of these strains will eventually generate random mutations within the DNA. Mutator strains suitable for use for in vivo mutagenesis are described in PCT Published Application WO 91/16427.

Variants may also be generated using cassette mutagenesis. In cassette mutagenesis a small region of a double stranded DNA molecule is replaced with a synthetic oligonucleotide "cassette" that differs from the native sequence. The oligonucleotide often contains completely and/or partially randomized native sequence.

Recursive ensemble mutagenesis may also be used to generate variants. Recursive ensemble mutagenesis is an algorithm for protein engineering (protein mutagenesis) developed to produce diverse populations of phenotypically related mutants whose members differ in amino acid sequence. This method uses a feedback mechanism to control successive rounds of combinatorial cassette mutagenesis. Recursive ensemble mutagenesis is described in Arkin, A.P. and Youvan, D.C., PNAS, USA, 89:7811-7815 (1992).

In some embodiments, variants are created using exponential ensemble mutagenesis. Exponential ensemble mutagenesis is a process for generating combinatorial libraries with a high percentage of unique and functional mutants, wherein small groups of residues are randomized in parallel to identify, at each altered position, amino acids which lead to functional proteins. Exponential ensemble mutagenesis is described in Delegrave, S. and Youvan, D.C., Biotechnology Research, 11:1548-1552 (1993). Random and site-directed mutagenesis are described in Arnold, F.H., Current Opinion in Biotechnology, 4:450-455 (1993).

In some embodiments, the variants are created using shuffling procedures wherein portions of a plurality of nucleic acids which encode distinct polypeptides are fused together to create chimeric nucleic acid sequences which encode chimeric polypeptides. Shuffling procedures are described in U.S. Patent Application Serial No. 08/677,112, filed July 9, 1996, U.S. Patent Application Serial No. 08/942,504, filed October 31, 1997, U.S. Patent No. 5,939,250, issued August 17, 1999, and U.S. Patent Application Serial No. 09/375,605, filed August 17, 1999.

The variants of the polypeptides of SEQ ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, and 80 may be (i) variants in which one or more of the amino acid residues of the polypeptides of SEQ ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, and 80 are substituted with a conserved or non-conserved amino acid residue (preferably a conserved amino acid residue) and such substituted amino acid residue may or may not be one encoded by the genetic code.

Conservative substitutions are those that substitute a given amino acid in a polypeptide by another amino acid of like characteristics. Typically seen as conservative substitutions are the following replacements: replacements of an aliphatic amino acid such as Ala, Val, Leu and Ile with another aliphatic amino acid; replacement of a Ser with a Thr or vice versa; replacement of an acidic residue such as Asp and Glu with another acidic residue; replacement of a residue bearing an amide group, such as Asp and Gln, with another residue bearing an amide group; exchange of a basic residue such as Lys and Arg with another basic residue; and replacement of an aromatic residue such as Phe, Tyr with another aromatic residue.

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Other variants are those in which one or more of the amino acid residues of the polypeptides of SEQ ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74 76, 78, and 80 includes a substituent group.

Still other variants are those in which the polypeptide is associated with another compound, such as a compound to increase the half-life of the polypeptide (for example, polyethylene glycol).

Additional variants are those in which additional amino acids are fused to the polypeptide, such as a leader sequence, a secretory sequence, a proprotein sequence or a sequence which facilitates purification, enrichment, or stabilization of the polypeptide.

In some embodiments, the fragments, derivatives and analogs retain the same biological function or activity as the polypeptides of SEO ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, and 80. In other embodiments, the fragment, derivative, or analog includes a proprotein, such that the fragment, derivative, or analog can be activated by cleavage of the proprotein portion to produce an active polypeptide.

Another aspect of the present invention are polypeptides or fragments thereof which have at least 70%, at least 80%, at least 85%, at least 90%, at least 95%, or more than 95% homology to one of the polypeptides of SEQ ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74 76, 78, and 80 or a fragment comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids thereof. Homology may be determined using a program, such as FASTA version 3.0t78 with the default parameters, which aligns the polypeptides or fragments being compared and determines the extent of amino acid identity or similarity between them. It will be appreciated that amino acid "homology" includes conservative amino acid substitutions such as those described above.

The polypeptides or fragments having homology to one of the polypeptides of SEQ ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74 76, 78, and 80 or a fragment comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids thereof may be obtained by isolating the nucleic acids encoding them using the techniques described above.

Alternatively, the homologous polypeptides or fragments may be obtained through biochemical enrichment or purification procedures. The sequence of potentially homologous polypeptides or fragments may be determined by proteolytic digestion, gel electrophoresis and/or microsequencing. The sequence of the prospective homologous polypeptide or fragment can be compared to one of the polypeptides of SEO ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74 76, 78, and 80 or a fragment comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids thereof using a program such as FASTA version 3.0t78 with the default parameters.

The polypeptides of SEQ ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, and 80 or fragments comprising at least 5,

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10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids thereof invention may be used in a variety of applications. For example, the polypeptides or fragments thereof may be used to catalyze biochemical reactions. In particular, the polypeptides of SEQ ID NOs: 14 and 46, which have homology to glutamate semialdehyde amino transferase, or fragments thereof, may be used to catalyze the synthesis of 5-aminolevulinate from S-4-amino-5-oxopentanoate. The polypeptides of SEQ ID NOs: 26 and 58, which have homology to triose phosphate isomerase, or fragments thereof, may be used to catalyze the synthesis of glycerone phosphate from D-glyceraldehyde 3-phosphate. The polypeptides of SEQ ID NOs: 32 and 64, which have homology to dCMP deaminase, or fragments thereof, may be used to catalyze the reaction of deoxyctidine and water to produce deoxyuridine and ammonia. The polypeptides of SEQ ID NOs: 38 and 72, which have homology to the MenA protein, or fragments thereof, may be used to catalyze the synthesis of menaquinone. The polypeptide of SEQ ID NO: 80, which has homology to glucose-1-dehydrogenase, may be used to catalyze the synthesis of D-glucono-1,5-lacctone from D-glucose.

The polypeptide of SEQ ID NO: 10, which has homology to lysyl tRNA synthetase, or fragments thereof, may be used to identify compounds capable of specifically inhibiting the growth of *Cenarchaeum symbiosis*, since tRNA synthetases are attractive targets for agents which inhibit growth.

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Agents which specifically inhibit the activity of the lysyl tRNA synthetase from *Cenarchaeum symbiosum* may be identified using a variety of methods known to those skilled in the art. For example, a plurality of agents may be generated using combinatorial chemistry or recombinant DNA libraries encoding a large number of short peptides. The lysyl tRNA synthetases from *Cenarchaeum symbiosum* and control organisms are contacted with the agents and those agents which bind to the lysyl tRNA synthetase from *Cenarchaeum symbiosum* but not to the enzyme from the control organisms are identified. *Cenarchaeum symbiosum* is then contacted with the identified agents to determine which agents inhibit the organism's growth.

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The polypeptides of SEQ ID NOs: 28 and 60, which have homology to the TATA box binding protein, or fragments thereof, may be used to identify promoters in nucleic acids from *Cenarchaeum symbiosis*. In such procedures, the polypeptide or fragment thereof is allowed to contact the nucleic acid and binding of the polypeptide or fragment thereof to the nucleic acid is detected. Binding may be detected by performing a gel shift analysis, a nuclease protection analysis, or by detecting the retention of the nucleic acid on a column matrix having the TATA box binding protein, or a fragment thereof, affixed thereto.

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Compounds which specifically inhibit the binding of the TATA box binding protein of *Cenarchaeum symbiosis* to promoters may also be used to inhibit growth of the organism. Such compounds may be identified as described above.

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Similarly, agents which specifically inhibit the activity of the polypeptides of SEO ID NOs: 34 and 68, which have homology to RNA helicase, may be used to inhibit the growth of *Cenarchaeum symbiosis*. Such agents may be identified as described above.

The polypeptides of SEO ID NOs: 30 and 62, which have homology to DNA polymerase I, or fragments thereof, may be used to insert a detectable label into a nucleic acid or to generate blunt ends on nucleic acids which have been digested with a restriction endonuclease.

The polypeptides of SEQ ID NOs: 42 and 78, which have homology to site specific DNA methyltranseferases, or fragments thereof, may be used in procedures in which it is desirable to protect nucleic acid sequences from digestion with restriction endonucleases. For example, a nucleic acid sequence having one or more restriction sites therein may be treated with the polypeptides of SEQ ID NOs: 42 or 76 prior to the addition of linkers to the nucleic acid. Thereafter, the linkers may be digested with the restriction enzyme, while the sites in the remainder of the nucleic acid are protected from digestion.

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The polypeptides of SEQ ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74 76, 78, and 80, or fragments comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids thereof, may also be used to generate antibodies which bind specifically to the polypeptides or fragments. The resulting antibodies may be used to determine whether a biological sample contains *Cenarchaeum symbiosum*. In such procedures, a biological sample is contacted with an antibody capable of specifically binding to one of the polypeptides of SEQ ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74 76, 78, and 80 or fragments comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids thereof. The ability of the biological sample to bind to the antibody is then determined. For example, binding may be determined by labeling the antibody with a detectable label such as a fluorescent agent, an enzymatic label, or a radioisotope. Alternatively, binding of the antibody to the sample may be detected using a secondary antibody having such a detectable label thereon. A variety of assay protocols which may be used to detect the presence of *Cenarchaeum symbiosum* in a sample are familiar to those skilled in the art. Particular assays include ELISA assays, sandwich assays, radioimmunoassays, and Western Blots.

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Polyclonal antibodies generated against the polypeptides of SEQ ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 58, 58, 60, 62, 64, 66, 68, 70, 72, 74 76, 78, and 80 or fragments comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids thereof can be obtained by direct injection of the polypeptides into an animal or by administering the polypeptides to an animal, preferably a nonhuman. The antibody so obtained will then bind the polypeptide itself. In this manner, even a sequence encoding only a fragment of the polypeptide can be used to generate antibodies which may bind to the whole native polypeptide. Such antibodies can then be used to isolate the polypeptide from cells expressing that polypeptide.

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For preparation of monoclonal antibodies, any technique which provides antibodies produced by continuous cell line cultures can be used. Examples include the hybridoma technique (Kohler and Milstein, 1975, Nature, 256:495-497), the trioma technique, the human B-cell hybridoma technique (Kozbor et al., 1983, Immunology Today 4:72), and the EBV-hybridoma technique (Cole, et al., 1985, in Monoclonal Antibodies and Cancer Therapy, Alan R.

Liss, Inc., pp. 77-96).

Techniques described for the production of single chain antibodies (U.S. Patent No. 4,946,778) can be adapted to produce single chain antibodies to the polypeptides of SEQ ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74 76, 78, and 80 or fragments comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids thereof. Alternatively, transgenic mice may be used to express humanized antibodies to these polypeptides or fragments thereof.

Antibodies generated against the polypeptides of SEO ID NOs: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, and 80 or fragments comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids thereof may be used in screening for similar polypeptides from other organisms and samples. In such techniques, polypeptides from the organism are contacted with the antibody and those polypeptides which specifically bind the antibody are detected. Any of the procedures described above may be used to detect antibody binding. One such screening assay is described in "Methods for Measuring Cellulase Activities", *Methods in Enzymology*, Vol 160, pp. 87-116.

As used herein the term "nucleic acid codes of SEQ ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45,

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57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77" encompasses the nucleotide sequences of SEQ ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77, fragments of SEQ ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77, nucleotide sequences homologous to SEO ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 or homologous to fragments of SEQ ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77, and sequences complementary to all of the preceding sequences. The fragments include portions of SEQ ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive nucleotides of SEQ ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77. Preferably, the fragments are novel fragments. Homologous sequences and fragments of SEQ ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 refer to a sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, 80%, 75% or 70% homology to these sequences. Homology may be determined using any of the computer programs and parameters described herein, including BLASTN version 2.0 with the default parameters. Homologous sequences also include RNA sequences in which uridines replace the thymines in the nucleic acid codes of SEQ ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77. The homologous

sequences may be obtained using any of the procedures described herein or may result from the correction of a sequencing error. It will be appreciated that the nucleic acid codes of SEQ ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 can be represented in the traditional single character format (See the inside back cover of Stryer, Lubert. *Biochemistry*, 3rd edition. W. H Freeman & Co., New York.) or in any other format which records the identity of the nucleotides in a sequence.

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As used herein the term "polypeptide codes of SEQ ID NOS. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60. 62. 64. 66. 68. 72. 76. 80. 4. 8. 12. 16. 18. 20. 22. 24. 36. 40. 44. 48. 50. 52. 54. 56. 70. 74. and 78" encompasses the polypeptide sequence of SEQ ID NOs. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78 which are encoded by the extended cDNAs of SEQ ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7. 11. 15. 17. 19. 21. 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77, polypeptide sequences homologous to the polypeptides of SEQ ID NOS. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78, or fragments of any of the preceding sequences. Homologous polypeptide sequences refer to a polypeptide sequence having at least 99%, 98%, 97%, 96%, 95%, 90%, 85%, 80%, 75% or 70% homology to one of the polypeptide sequences of SEQ ID NOS. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78. Homology may be determined using any of the computer programs and parameters described herein, including FASTA version 3.0t78 with the default parameters or with any modified parameters. The homologous sequences may be obtained using any of the procedures described herein or may result from the correction of a sequencing error. The polypeptide fragments comprise at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids of the polypeptides of SEQ ID NOS. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78. Preferably, the fragments are novel fragments. It will be appreciated that the polypeptide codes of the SEQ ID NDS. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78 can be represented in the traditional single character format or three letter format (See the inside back cover of Starrier, Lubert. Biochemistry, 3rd edition. W. H Freeman & Co., New York.) or in any other format which relates the identity of the polypeptides in a sequence.

It will be appreciated by those skilled in the art that the nucleic acid codes of SEQ ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 and polypeptide codes of SEQ ID NOS. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78 can be stored, recorded, and manipulated on any medium which can be read and accessed by a computer. As used herein, the words "recorded" and "stored" refer to a process for storing information on a computer medium. A skilled artisan can readily adopt any of the presently known methods for recording information on a computer readable medium to generate manufactures comprising one or more of the nucleic acid codes of SEQ ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37,

41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77, one or more of the polypeptide codes of SEO ID NOS. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78. Another aspect of the present invention is a computer readable medium having recorded thereon at least 2, 5, 10, 15, or 20 nucleic acid codes of SEO ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77.

Another aspect of the invention is a computer readable medium having recorded thereon one or more of the nucleic acid codes of SEO ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, and 79. Another aspect of the present invention is a computer readable medium having recorded thereon at least 2, 5, 10, or 15 of SEO ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, and 79.

Another aspect of the present invention is a computer readable medium having recorded thereon one or more of the nucleic acid codes of SEQ ID NOs. 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77. Another aspect of the present invention is a computer readable medium having recorded thereon at least 2, 5, 10, or 15 of SEQ ID NOs. 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77.

Another aspect of the present invention is a computer readable medium having recorded thereon one or more of the polypeptide codes of SEQ ID NOS. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78. Another aspect of the present invention is a computer readable medium having recorded thereon one or more of the the polypeptide codes of SEQ ID NOS. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, and 80. Another aspect of the present invention is a computer readable medium having recorded thereon one or more of the the polypeptide codes of SEQ ID NOS. 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78.

Another aspect of the present invention is a computer readable medium having recorded thereon at least 2, 5, 10, 15, or 20 polypeptide codes of SEO ID NOS. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78. Another aspect of the present invention is a computer readable medium having recorded thereon at least 2, 5, 10, or 15 polypeptide codes of SEO ID NOS. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, and 80. Another aspect of the present invention is a computer readable medium having recorded thereon at least 2, 5, 10, or 15 polypeptide codes of SEO ID NOS. 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78.

Computer readable media include magnetically readable media, optically readable media, electronically readable media and magnetic/optical media. For example, the computer readable media may be a hard disk, a floppy disk, a magnetic tape, CD-ROM, Digital Versatile Disk (DVD), Random Access Memory (RAM), or Read Only Memory (ROM) as well as other types of other media known to those skilled in the art.

Embodiments of the present invention include systems, particularly computer systems which store and manipulate the sequence information described herein. One example of a computer system 100 is illustrated in block diagram form in Figure 3. As used herein, "a computer system" refers to the hardware components, software components,

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and data storage components used to analyze the nucleotide sequences of the nucleic acid codes of SEO ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 or the sequences of the polypeptide codes of 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78. The computer system 100 preferably includes a processor for processing, accessing and manipulating the sequence data. The processor 105 can be any well-known type of central processing unit, such as the Pentium III from Intel Corporation, or similar processor from Sun, Motorola, Compaq or International Business Machines.

Preferably, the computer system 100 is a general purpose system that comprises the processor 105 and one or more internal data storage components 110 for storing data, and one or more data retrieving devices for retrieving the data storage components. A skilled artisan can readily appreciate that any one of the currently available computer systems are suitable.

In one particular embodiment, the computer system 100 includes a processor 105 connected to a bus which is connected to a main memory 115 (preferably implemented as RAM) and one or more internal data storage devices 110, such as a hard drive and/or other computer readable media having data recorded thereon. In some embodiments, the computer system 100 further includes one or more data retrieving device 118 for reading the data stored on the internal data storage devices 110.

The data retrieving device 118 may represent, for example, a floppy disk drive, a compact disk drive, a magnetic tape drive, etc. In some embodiments, the internal data storage device 110 is a removable computer readable medium such as a floppy disk, a compact disk, a magnetic tape, etc. containing control logic and/or data recorded thereon. The computer system 100 may advantageously include or be programmed by appropriate software for reading the control logic and/or the data from the data storage component once inserted in the data retrieving device.

The computer system 100 includes a display 120 which is used to display output to a computer user. It should also be noted that the computer system 100 can be linked to other computer systems 125a·c in a network or wide area network to provide centralized access to the computer system 100.

Software for accessing and processing the nucleotide sequences of the nucleic acid codes of SEQ ID Nos.1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 or the polypeptide codes of SEQ ID Nos. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78 (such as search tools, compare tools, and modeling tools etc.) may reside in main memory 115 during execution.

In some embodiments, the computer system 100 may further comprise a sequence comparer for comparing the above-described nucleic acid codes of SEO ID Nos. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 or the polypeptide codes of SEO ID Nos. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78 stored on a computer readable medium to reference nucleotide or polypeptide sequences stored on a computer readable medium. A "sequence comparer" refers to one or more programs

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which are implemented on the computer system 100 to compare a nucleotide sequence with other nucleotide sequences and/or compounds stored within the date storage means. For example, the sequence comparer may compare the nucleotide sequences of the nucleic acid codes of SEO ID Nos. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 or the polypeptide codes of SEO ID Nos. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78 stored on a computer readable medium to reference sequences stored on a computer readable medium to identify homologies or structural motifs. Various sequence comparer programs identified elsewhere in this patent specification are particularly contemplated for use in this aspect of the invention. Protein and/or nucleic acid sequence homologies may be evaluated using any of the variety of sequence comparison algorithms and programs known in the art. Such algorithms and programs include, but are by no means limited to, TBLASTN, BLASTN, BLASTP, FASTA, TFASTA, and CLUSTALW (Pearson and Lipman, 1988, *Proc. Natl. Acad. Sci. USA 85*(8):2444-2448; Altschul *et al.*, 1990, *J. Mol. Biol. 215*(3):403-410; Thompson *et al.*, 1994, *Nucleic Acids Res. 22*(2):4673-4680; Higgins *et al.*, 1999, *Methods Enzymol. 266*:383-402; Altschul *et al.*, 1990, *J. Mol. Biol. 215*(3):403-410; Altschul *et al.*, 1993, *Nature Genetics 3*:266-272).

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In one embodiment, protein and nucleic acid sequence homologies are evaluated using the Basic Local Alignment Search Tool ("BLAST") which is well known in the art (see, e.g., Karlin and Altschul, 1990, Proc. Natl. Acad. Sci. USA 87:2267-2268; Altschul et al., 1990, J. Mol. Biol. 215:403-410; Altschul et al., 1993, Nature Genetics 3:266-272; Altschul et al., 1997, Nuc. Acids Res. 25:3389-3402). In particular, five specific BLAST programs are used to perform the following task:

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- BLASTP and BLAST3 compare an amino acid query sequence against a protein sequence database;
- BLASTN compares a nucleotide query sequence against a nucleotide sequence database;
- (3) BLASTX compares the six-frame conceptual translation products of a query nucleotide sequence (both strands) against a protein sequence database;
- (4) TBLASTN compares a query protein sequence against a nucleotide sequence database translated in all six reading frames (both strands); and
- (5) TBLASTX compares the six-frame translations of a nucleotide query sequence against the six-frame translations of a nucleotide sequence database.

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The BLAST programs identify homologous sequences by identifying similar segments, which are referred to herein as "high-scoring segment pairs," between a query amino or nucleic acid sequence and a test sequence which is preferably obtained from a protein or nucleic acid sequence database. High-scoring segment pairs are preferably identified (i.e., aligned) by means of a scoring matrix, many of which are known in the art. Preferably, the scoring matrix used is the BLOSUM62 matrix (Gonnet et al., 1992, Science 256:1443-1445; Henikoff and Henikoff, 1993, Proteins 17:49-61). Less preferably, the PAM or PAM250 matrices may also be used (see, e.g., Schwartz and

Dayhoff, eds., 1978, Matrices for Detecting Distance Relationships: Atlas of Protein Sequence and Structure, Washington: National Biomedical Research Foundation). BLAST programs are accessible through the U.S. National Library of Medicine, e.g., at www.ncbi.nlm.nih.gov.

The BLAST programs evaluate the statistical significance of all high-scoring segment pairs identified, and preferably selects those segments which satisfy a user-specified threshold of significance, such as a user-specified percent homology. Preferably, the statistical significance of a high-scoring segment pair is evaluated using the statistical significance formula of Karlin (see, e.g., Karlin and Altschul, 1990, *Proc. Natl. Acad. Sci. USA 87*:2267-2268).

The parameters used with the above algorithms may be adapted depending on the sequence length and degree of homology studied. In some embodiments, the parameters may be the default parameters used by the algorithms in the absence of instructions from the user.

Figure 4 is a flow diagram illustrating one embodiment of a process 200 for comparing a new nucleotide or protein sequence with a database of sequences in order to determine the homology levels between the new sequence and the sequences in the database. The database of sequences can be a private database stored within the computer system 100, or a public database such as GENBANK that is available through the Internet.

The process 200 begins at a start state 201 and then moves to a state 202 wherein the new sequence to be compared is stored to a memory in a computer system 100. As discussed above, the memory could be any type of memory, including RAM or an internal storage device.

The process 200 then moves to a state 204 wherein a database of sequences is opened for analysis and comparison. The process 200 then moves to a state 206 wherein the first sequence stored in the database is read into a memory on the computer. A comparison is then performed at a state 210 to determine if the first sequence is the same as the second sequence. It is important to note that this step is not limited to performing an exact comparison between the new sequence and the first sequence in the database. Well-known methods are known to those of skill in the art for comparing two nucleotide or protein sequences, even if they are not identical. For example, gaps can be introduced into one sequence in order to raise the homology level between the two tested sequences. The parameters that control whether gaps or other features are introduced into a sequence during comparison are normally entered by the user of the computer system.

Once a comparison of the two sequences has been performed at the state 210, a determination is made at a decision state 210 whether the two sequences are the same. Of course, the term "same" is not limited to sequences that are absolutely identical. Sequences that are within the homology parameters entered by the user will be marked as "same" in the process 200.

If a determination is made that the two sequences are the same, the process 200 moves to a state 214 wherein the name of the sequence from the database is displayed to the user. This state notifies the user that the sequence with the displayed name fulfills the homology constraints that were entered. Once the name of the stored sequence is displayed to the user, the process 200 moves to a decision state 218 wherein a determination is made whether more sequences exist

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in the database. If no more sequences exist in the database, then the process 200 terminates at an end state 220. However, if more sequences do exist in the database, then the process 200 moves to a state 224 wherein a pointer is moved to the next sequence in the database so that it can be compared to the new sequence. In this manner, the new sequence is aligned and compared with every sequence in the database.

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It should be noted that if a determination had been made at the decision state 212 that the sequences were not homologous, then the process 200 would move immediately to the decision state 218 in order to determine if any other sequences were available in the database for comparison.

Accordingly, one aspect of the present invention is a computer system comprising a processor, a data

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storage device having stored thereon a nucleic acid code of SEQ ID Nos. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 or the polypeptide codes of SEO ID NOs. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78, a data storage device having retrievably stored thereon reference nucleotide sequences or polypeptide sequences to be compared to the nucleic acid code of SEQ ID Nos.1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 or the polypeptide codes of SEQ ID NOs. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78 and a sequence comparer for conducting the comparison. The sequence comparer may indicate a homology level between the sequences compared or identify structural motifs in the above described nucleic acid code of SEQ ID Nos. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19. 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 or the polypeptide codes of SEQ ID NOs. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78 or it may identify structural motifs in sequences which are compared to these nucleic acid codes and polypeptide codes. In some embodiments, the data storage device may have stored thereon the sequences of at least 2, 5, 10, 15, 20, 25, 30 or 40 or more of the nucleic acid codes of SEQ ID Nos. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 or the polypeptide codes of SEO ID NDs. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72,

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Another aspect of the present invention is a method for determining the level of homology between a nucleic acid code of SEO ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 or the polypeptide codes of SEO ID NOs. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78 and a reference nucleotide sequence or polypeptide sequence, comprising the steps of reading the nucleic acid code or the polypeptide code and the reference nucleotide or polypeptide sequence through the use of a computer program which determines homology levels and determining homology between the nucleic acid code or polypeptide code and the reference nucleotide or polypeptide sequence with the computer program. The computer program

76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 58, 70, 74, and 78.

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may be any of a number of computer programs for determining homology levels, including those specifically enumerated herein, including BLAST2N or BLASTN with the default parameters or with any modified parameters. The method may be implemented using the computer systems described above. The method may also be performed by reading at least 2, 5, 10, 15, 20, 25, 30 or 40 or more of the above described nucleic acid codes of SEQ ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 or the polypeptide codes of SEQ ID NOs. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78 through use of the computer program and determining homology between the nucleic acid codes or polypeptide codes and reference nucleotide sequences or polypeptide sequences.

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Figure 5 is a flow diagram illustrating one embodiment of a process 250 in a computer for determining whether two sequences are homologous. The process 250 begins at a start state 252 and then moves to a state 254 wherein a first sequence to be compared is stored to a memory. The second sequence to be compared is then stored to a memory at a state 256. The process 250 then moves to a state 260 wherein the first character in the first sequence is read and then to a state 262 wherein the first character of the second sequence is read. It should be understood that if the sequence is a nucleotide sequence, then the character would normally be either A, T, C, G or U. If the sequence is a protein sequence, then it is preferably in the single letter amino acid code so that the first and sequence sequences can be easily compared.

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A determination is then made at a decision state 264 whether the two characters are the same. If they are the same, then the process 250 moves to a state 268 wherein the next characters in the first and second sequences are read. A determination is then made whether the next characters are the same. If they are, then the process 250 continues this loop until two characters are not the same. If a determination is made that the next two characters are not the same, the process 250 moves to a decision state 274 to determine whether there are any more characters either sequence to read.

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If there aren't any more characters to read, then the process 250 moves to a state 276 wherein the level of homology between the first and second sequences is displayed to the user. The level of homology is determined by calculating the proportion of characters between the sequences that were the same out of the total number of sequences in the first sequence. Thus, if every character in a first 100 nucleotide sequence aligned with a every character in a second sequence, the homology level would be 100%.

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Alternatively, the computer program may be a computer program which compares the nucleotide sequences of the nucleic acid codes of the present invention, to reference nucleotide sequences in order to determine whether the nucleic acid code of SEQ ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 differs from a reference nucleic acid sequence at one or more positions. Optionally such a program records the length and identity of inserted, deleted or substituted nucleotides with respect to the sequence of either the reference polynucleotide or the nucleic acid code of SEQ ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49,

51, 53, 55, 69, 73 and 77. In one embodiment, the computer program may be a program which determines whether the nucleotide sequences of the nucleic acid codes of SEQ ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 contain a single nucleotide polymorphism (SNP) with respect to a reference nucleotide sequence.

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Accordingly, another aspect of the present invention is a method for determining whether a nucleic acid code of SEQ ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 differs at one or more nucleotides from a reference nucleotide sequence comprising the steps of reading the nucleic acid code and the reference nucleotide sequence through use of a computer program which identifies differences between nucleic acid sequences and identifying differences between the nucleic acid code and the reference nucleotide sequence with the computer program. In some embodiments, the computer program is a program which identifies single nucleotide polymorphisms. The method may be implemented by the computer systems described above and the method illustrated in Figure 6. The method may also be performed by reading at least 2, 5, 10, 15, 20, 25, 30, or 40 of the nucleic acid codes of SEQ ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 and the reference nucleotide sequences through the use of the computer program and identifying differences between the nucleic acid codes and the reference nucleotide sequences with the computer program.

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In other embodiments the computer based system may further comprise an identifier for identifying features within the nucleotide sequences of the nucleic acid codes of SEQ ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 or the polypeptide codes of SEQ ID NOs. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78.

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An "identifier" refers to one or more programs which identifies certain features within the above-described nucleotide sequences of the nucleic acid codes of SEO ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 or the polypeptide codes of SEO ID NOs. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78. In one embodiment, the identifier may comprise a program which identifies an open reading frame in the nucleic acid codes of SEO ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77.

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Figure 7 is a flow diagram illustrating one embodiment of an identifier process 300 for detecting the presence of a feature in a sequence. The process 300 begins at a start state 302 and then moves to a state 304 wherein a first sequence that is to be checked for features is stored to a memory 115 in the computer system 100. The process 300 then moves to a state 306 wherein a database of sequence features is opened. Such a database would include a list of each feature's attributes along with the name of the feature. For example, a feature name

could be "Initiation Codon" and the attribute would be "ATG". Another example would be the feature name "TAATAA Box" and the feature attribute would be "TAATAA". An example of such a database is produced by the University of Wisconsin Genetics Computer Group (www.gcg.com). Alternatively, the features may be structural polypeptide motifs such as alpha helices, beta sheets, or functional polypeptide motifs such as enzymatic active sites, helix-turn-helix motifs or other motifs known to those skilled in the art.

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Once the database of features is opened at the state 306, the process 300 moves to a state 308 wherein the first feature is read from the database. A comparison of the attribute of the first feature with the first sequence is then made at a state 310. A determination is then made at a decision state 316 whether the attribute of the feature was found in the first sequence. If the attribute was found, then the process 300 moves to a state 318 wherein the name of the found feature is displayed to the user.

The process 300 then moves to a decision state 320 wherein a determination is made whether move features exist in the database. If no more features do exist, then the process 300 terminates at an end state 324. However, if more features do exist in the database, then the process 300 reads the next sequence feature at a state 326 and loops back to the state 310 wherein the attribute of the next feature is compared against the first sequence.

It should be noted, that if the feature attribute is not found in the first sequence at the decision state 316, the process 300 moves directly to the decision state 320 in order to determine if any more features exist in the database.

Accordingly, another aspect of the present invention is a method of identifying a feature within the nucleic acid codes of SEO ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 or the polypeptide codes of SEO ID NOs. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78 comprising reading the nucleic acid code(s) or polypeptide code(s) through the use of a computer program which identifies features therein and identifying features within the nucleic acid code(s) with the computer program. In one embodiment, computer program comprises a computer program which identifies open reading frames. The method may be performed by reading a single sequence or at least 2, 5, 10, 15, 20, 25, 30, or 40 of the nucleic acid codes of SEO ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 or the polypeptide codes of SEO ID NOs. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78 through the use of the computer program and identifying features within the nucleic acid codes or polypeptide codes with the computer program.

The nucleic acid codes of SEO ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 or the polypeptide codes of SEO ID NOs. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78 may be stored and manipulated in a variety of data processor programs in a variety of formats. For example, the nucleic acid codes of SEO ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33,

37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 or the polypeptide codes of SEQ ID NOs. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78 may be stored as text in a word processing file, such as MicrosoftWORD or WORDPERFECT or as an ASCII file in a variety of database programs familiar to those of skill in the art, such as DB2, SYBASE, or ORACLE. In addition, many computer programs and databases may be used as sequence comparers, identifiers, or sources of reference nucleotide sequences or polypeptide sequences to be compared to the nucleic acid codes of SEQ ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 or the polypeptide codes of SEQ ID NOs. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78. The following list is intended not to limit the invention but to provide guidance to programs and databases which are useful with the nucleic acid codes of SEQ ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 or the polypeptide codes of SEQ ID NOs. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78.

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The programs and databases which may be used include, but are not limited to: MacPattern (EMBL), DiscoveryBase (Molecular Applications Group), GeneMine (Molecular Applications Group), Look (Molecular Applications Group), MacLook (Molecular Applications Group), BLAST and BLAST2 (NCBI), BLASTN and BLASTX (Altschul et al., *J. Mol. Biol.* 215: 403 (1990)), FASTA (Pearson and Lipman, *Proc. Natl. Acad. Sci. USA*, 85: 2444 (1988)), FASTDB (Brutlag et al. Comp. App. Biosci. 6:237-245, 1990), Catalyst (Molecular Simulations Inc.), Catalyst/SHAPE (Molecular Simulations Inc.), Lerius².DBAccess (Molecular Simulations Inc.), HypoGen (Molecular Simulations Inc.), Insight II, (Molecular Simulations Inc.), Discover (Molecular Simulations Inc.), CHARMm (Molecular Simulations Inc.), Felix (Molecular Simulations Inc.), DelPhi, (Molecular Simulations Inc.), QuanteMM, (Molecular Simulations Inc.), Homology (Molecular Simulations Inc.), Modeler (Molecular Simulations Inc.), ISIS (Molecular Simulations Inc.), Quanta/Protein Design (Molecular Simulations Inc.), WebLab (Molecular Simulations Inc.), SeqFold (Molecular Simulations Inc.), the MDL Available Chamicals Directory database, the MDL Drug Data Report data base, the Comprehensive Medicinal Chemistry database, Derwents's World Drug Index database, the BioByteMasterFile database, the Genbank database, and the Genseqn database. Many other programs and data bases would be apparent to one of skill in the ert given the present disclosure.

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Motifs which may be detected using the above programs include sequences encoding leucine zippers, helixturn-helix motifs, glycosylation sites, ubiquitination sites, alpha helices, and beta sheets, signal sequences encoding signal peptides which direct the secretion of the encoded proteins, sequences implicated in transcription regulation such as homeoboxes, acidic stretches, enzymatic active sites, substrate binding sites, and enzymatic cleavage sites.

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The present invention will be further described with reference to the following examples; however, it is to be understood that the present invention is not limited to such examples.

In order to begin the physiological characterization of *Cenarchaeum symbiosum*, it was necessary to obtain enriched preparations of *Cenarchaeum symbiosum* for use in the construction of genomic DNA libraries in fosmid based vectors. Genomic DNA libraries were constructed from two enriched preparations using the methods described in Example 1 below.

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Example 1

Enrichment of Cenarchaeum symbiosum Cells

in Samples Obtained from Axinella Mexicana

Enriched preparations of *Cenarchaeum symbiosum* for use in the preparation of the first fosmid genomic DNA library were obtained essentially as described in Preston, C. M. et al. 1996. A psychrophilic crenarchaeon inhabits a marine sponge: Cenarchaeum symbiosum gen. nov., sp. nov. *Proc. Natl. Acad. Sci.* USA 93, 6241-6246. Briefly, a small individual of *A. mexicana* was incubated in calcium- and magnesium-free artificial seawater (ASW) containing 0.25 mg/ml Pronase. The tissue was then homogenized and enriched for archaeal cells by differential centrifugation.

Enriched preparations of *Cenarchaeum symbiosum* for use in preparing the second fosmid genomic DNA library were obtained from a different sponge individual using the following improved enrichment procedure. A small individual of *A. mexicana* was incubated in calcium- and magnesium-free artificial seawater (460mm NaCl, 11mM KCl, 7mM Na₂SO₄, 2mM NaHCO₃) containing 0.25 mg/ml Pronase at room temperature for one hour. The sponge tissue was rinsed in artificial seawater and homogenized in a blender. Large particles and spicules were removed by low-speed centrifugation (4000 rpm, Sorvall GSA rotor at 4°C). The supernatant was next centrifuged at 5000 rpm for 5 min. at 4°C to remove large sponge cells, and the resulting supernatant was centrifuged at 10,000 rpm in a GSA rotor at 4°C for 20 min. to collect the *Cenarchaeum symbiosum* cells. Following centrifugation, the recovered cell fraction containing *Cenarchaeum symbiosum* was further incubated for 1 hr at 4°C in 10 mM Tris/HCl pH 8 and 200 mM EDTA. The cells were then pelleted and subsequently purified on a 15 % Percoll (Sigma) cushion in artificial sea water centrifuged at 2500 rpm in a Beckman SS34 rotor. Archaeal cells banded in the light, upper fraction after centrifugation. This cell fraction was washed in ASW and resuspended in TE buffer (10 mM TrisHCl pH 8, 0.1 mM EDTA). The additional incubation step was found to increase the lysis of sponge cells, which resulted in an enhanced separation of archaeal and eukaryotic cells in the percoll gradient.

Quantitative hybridization experiments were performed as described in DeLong, E. F. 1992. Archaea in coastal marine environments. *Proc. Natl. Acad. Sci.* 89, 5685-5689 using an oligonucleotide specific for archaea having the sequence GTGCTCCCCGCCAATTCCT (SEQ ID NO: 115). These hybridization experiments indicated that 25% to 30% of the total rRNA from this fraction was derived from archaea.

The enriched cell preparations were then utilized to construct fosmid libraries as described in Example 2 below.

Example 2

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Construction of Fosmid Libraries

DNA was extracted from the enriched preparations of Example 1 and inserted into fosmids as described in Preston, C. M. et al. 1996. A psychrophilic crenarchaeon inhabits a marine sponge: Cenarchaeum symbiosum gen. nov., sp. nov. Proc. Natl. Acad. Sci. USA 93, 6241-6246 and Stein, J.L. et al. 1996. Characterization of uncultivated prokaryotes: isolation and analysis of a 40-kilobase-pair genome fragment from a planktonic marine archaeon. J. Bacteriol, 178, 591-599. A vertical cross section of sponge (0.5 g) was mechanically dissociated in 0.22 \(\mu \) filtered, autoclaved seawater using a tissue homogenizer. Cell lysis was accomplished by incubating the dissociated cells in 1 mg of lysozyme per ml for 30 min. at 37°C followed by an incubation for 30 min. at 55°C with 0.5mg of proteinase K per ml and 1% SDS. The tubes were finally placed in a boiling water bath for 60 sec to complete lysis. The protein fraction was removed with two extractions with phenol:chloroform:isoamyl alcohol (50:49:1), pH 8.0, followed by a chloroform: isoamyl alcohol (24:1) extraction. Nucleic acids were ethanol-precipitated and resuspended in TE buffer (10mM Tris.HCI/1mM Na₂-EDTA, pH 8.0). Approximately 5µg of DNA was purified by CsCl equilibrium density gradiant ultracentriguation on a Beckman Optima tabletop ultracentrifuge using a TLA100 rotor. genomic DNA obtained above was inserted into fosmids as follows. The genomic DNA was partially digested with Sau3Al (Promega) and treated with heat-labile phosphatase (HK phosphatase; Epicentre). The partially digested genomic DNA was ligated with pFOS (See U.J. Kim et al., Nucleic Acids Res. 20:1083-1085 (1992)) which had previously been digested with Aatll, phosphatase treated (HK phosphatase), and subsequently digested with BamHl. The ligation mixture was used for in vitro packaging with the Gigapack XL packaging system (Stratagene) selecting for DNA inserts of 35 to 45kb. The phage particles were transfected into E. coli DH10B (Bethesda Research LaboratoriesP and the cells were spread onto LB plates supplemented with 12.5µg/ml chloramphenicol.

Example 3

Identification of Fosmids Containing the Cenarchaeum symbiosum rRNA Operon

The fosmid libraries constructed above were screened to identify clones containing the rRNA operon. PCR reactions were conducted on the library using primers known to amplify the rRNA operon.

The first fosmid library yielded seven unique clones, out of a total of 10,236 recombinant fosmids, which contained the *Cenarchaeum symbiosum* rRNA operon. The second fosmid library yielded eight unique clones, out of a total of 2100 recombinant fosmids, which contained the *Cenarchaeum symbiosum* rRNA operon.

The sequences of the 16S rRNA genes in each of the 15 fosmids containing the *Cenarchaeum symbiosum* rRNA operon were determined. The sequences of the small subunit rRNA genes of these 15 fosmids exhibited variations with respect to one another. Ten of the fosmids contained a small subunit rRNA gene having the sequence of the 16S rRNA gene in the insert of SEQ ID NO: 1, while the remaining fosmids contained a small subunit rRNA gene having the sequence of the 16S rRNA gene in the insert of SEQ ID NO: 2. As discussed in more detail below, the differences in the sequences of the rRNA genes may be used to determine whether a sample contains *Cenarchaeum symbiosum* variant A or *Cenarchaeum symbiosum* variant B.

In addition to determining the sequences of the rRNA genes, the sequences adjacent to the rRNA genes were also determined.

Example 4

Fosmid Sequencing

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Partial restriction enzyme digests were conducted on two purified fosmids, fosmid 101G10 (which contains the variant A sequence) and fosmid 60A5 (which contains the variant B sequence). The partially digested DNA was used to construct plasmid libraries containing inserts of 1-2 kb. The resulting plasmids were sequenced using Applied Biosystems (ABI, Foster City, CA) Prism Dye-terminator FS reaction mix. Direct sequencing from fosmids was used for gap filling and resequencing to ensure accuracy. Fosmid sequencing was performed by using DNA from a single 3 ml overnight culture purified on an Autogen 740 automated plasmid isolation system. Each reaction consisted of one preparation of DNA directly resuspended by the addition of 16 μ l H₂O, 8 μ l oligonucleotide primer (1.4 pmol/ μ l) and 16 μ l ABI Prism Dye-terminator FS reaction mix. Cycle sequencing was performed with a 96° C 3 min. preincubation followed by 25 cycles of the sequence 96° C 20 sec. / 50° C 20 sec. / 60° C 4 min. and a 5 min. post-cycling incubation at 60° C. Sequencing reaction products were analyzed on ABI 377 Prism Sequencers.

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The complete sequences of the *Cenarchaeum symbiosum* derived inserts in the two fosmids are provided in the accompanying sequence listing as SEO ID NO: 1 (fosmid 101G10) and SEO ID NO: 2 (fosmid 60A5). The insert of fosmid 101G10 (SEO ID NO: 1, designated variant A) was 32,998 bp and was syntenic over ca. 28 kbp with the 42,432 bp insert of fosmid 60A5 (SEO ID NO:2, designated variant B). Analysis of the common 28 kbp region is shown in Fig. 1.

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Although the sequences of both fosmids could be aligned unambiguously over most of the overlapping region, four large insertion/deletions ranging in size from 142 bp to 1994 bp were identified between positions 20,500 and 25,800. The longest insertion contained a repetitive element of 1784 bp, that was found in the sequence of SEQ ID NO: 1 between *men*A and ORFO5. It was composed of a 3-fold direct repeat of 575 bp (rep1 through 3 in Fig. 1), with repeats exhibiting only minor sequence variation (95.8% to 98.7% identity).

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A segment of 56 bp at the start of this repeat was also found adjacent to the 3' terminus of the third direct repeat. No obvious structural or sequence similarities to known repeats or mobile genetic elements from other organisms were identified within the repeat sequence. Its occurrence in only one variant and its relatively low G+C content relative to the rest of the fragment suggest that it may have been acquired by horizontal transfer from a different genetic context.

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The sequenced regions contained several open reading frames or RNA encoding sequences. Some of the identified open reading frames encode proteins having homology to previously identified proteins. In particular, some of the open reading frames encode proteins involved in several metabolic pathways, providing insight into the physiology of *Cenarchaeum symbiosum*.

An open reading frame which encodes a protein having homology to glutamate semialdehyde aminotransferase (a protein involved in heme biosynthesis) was identified between nucleotides 7604-8908 of the

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insert from fosmid 101G10 (SEQ ID NO: 1) and between nucleotides 23558-24682 of the insert from fosmid 60A5 (SEQ ID NO: 2). These open reading frames have been assigned SEQ ID NOs: 45 and 13 respectively in the accompanying sequence listing, while the polypeptides they encode have been assigned SEQ ID NOs: 46 and 14 respectively in the accompanying sequence listing. A gene encoding glutamate semialdehyde aminotransferase has also been detected in a rRNA operon containing genomic fragment of a planktonic marine crenarchaeote. (Stein, J.L. et al. 1996. Characterization of uncultivated prokaryotes: isolation and analysis of a 40-kilobase-pair genome fragment from a planktonic marine archaeon. J. Bacteriol. 178, 591-599)

An open reading frame encoding a protein having homology to triose-phosphate isomerase was identified between 13944-14612 of the insert from fosmid 101G10 (SEQ ID NO: 1) and between nucleotides 29655-30491 of the insert from fosmid 60A5 (SEQ ID NO: 2). These open reading frames have been assigned SEQ ID NOs: 57 and 25 respectively in the accompanying sequence listing, while the polypeptides they encode have been assigned SEQ ID NOs: 58 and 26 respectively in the accompanying sequence listing. This triosephosphate isomerase represents the first such protein sequence reported in a crenarchaeote, and shares known archaeal signature sequences and deletions which distinguish archaeal triosephosphate isomerase genes from their eucaryal and eubacterial homologues.

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An open reading frame encoding a protein having homology to the TATA binding protein was identified between 14616-15164 of the insert from fosmid 101G10 (SEQ ID NO: 1) and between nucleotides 30501-31049 of the insert from fosmid 60A5 (SEQ ID NO: 2) on the strands complementary to the insert strands provided in SEQ ID NOs: 1 and 2. These open reading frames have been assigned SEQ ID NOs: 59 and 27 respectively in the accompanying sequence listing, while the polypeptides they encode have been assigned SEQ ID NOs: 60 and 28 respectively in the companying sequence listing. This TATA box-binding protein (TBP) is similar to other known archaeal TBP's and is N-terminally truncated with respect to the eukaryal homologs. It shares 49% amino acid similarity with TBP from *Pyrococcus woesii*.

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An open reading frame encoding a protein having homology to DNA polymerase (a protein involved in DNA replication and repair) was identified between nucleotides 15488-18025 of the insert from fosmid 101G10 (SEQ ID NO: 1) and between nucleotides 31371-33905 of the insert from fosmid 60A5 (SEQ ID NO: 2) on the strands complementary to the insert strands provided in SEQ ID NOs: 1 and 2. These open reading frames have been assigned SEQ ID NOs: 61 and 29 respectively in the accompanying sequence listing, while the polypeptides they encode have been assigned SEQ ID NOs: 62 and 30 respectively in the accompanying sequence listing.

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The DNA polymerase of *Cenarchaeum symbiosum* has a high degree of similarity to the crenarchaeal homologs from the extreme thermophiles *Sulfolobus acidocaldarius* and *Pyrodictium occultum* (54% and 53% resp.) and exhibits all conserved motifs of B-(a-)type DNA polymerases and 3'-5'-exonuclease motifs, both indicative of archaeal polymerases. A more detailed phylogenetic analysis and biochemical characterization of the *C. symbiosum* polymerase has been published elsewhere. (Schleper, C., *et al.* 1997. Characterization of a DNA polymerase from the uncultivated psychrophilic archaeon *Cenarchaeum symbiosum*. *J. Bact.* 179, 7803-7811)

An open reading frame which encodes a protein having homology to dCMP deaminase (a protein involved in pyrimidine synthesis) was identified between nucleotides 18022-18663 of the insert from fosmid 101610 (SEQ ID NO: 1) and between nucleotides 33902-34456 of the insert from fosmid 60A5 (SEQ ID NO: 2) on the strands complementary to the insert strands provided in SEQ ID NOs: 1 and 2. These open reading frames have been assigned SEQ ID NOs: 63 and 31 respectively in the accompanying sequence listing, while the polypeptides they encode have been assigned SEQ ID NOs: 64 and 32 respectively in the accompanying sequence listing.

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An open reading frame encoding a protein having homology to the ATP dependent RNA helicase (a protein involved in translation) was identified between nucleotides 18638-20149 of the insert from fosmid 101610 (SEQ ID NO: 1) and between nucleotides 34559-36067 of the insert from fosmid 60A5 (SEQ ID NO: 2). These open reading frames have been assigned SEQ ID NOs: 65 and 33 respectively in the accompanying sequence listing, while the polypeptides they encode have been assigned SEQ ID NOs: 66 and 34 respectively in the accompanying sequence listing. The identified ATP RNA helicase is highly similar in sequence to homologues found in the genomic sequences of three euryarchaeota (Bult, C., et al. Complete genome sequence of the methanogenic archaeon, Methanococcus jannaschii. Science 273, 1058-1073; Klenk, H.P. et al. 1997. The complete genome sequence of the hyperthermophilic, sulphate-reducing archaeon Archaeoglobus fulgidus. Nature 390, 364-370; Smith, D. R.et al. 1997. Complete genome sequence of Methanobacterium thermoautotrophicum delta H: functional analysis and comparative genomics. J. Bacteriol. 179, 7135-7155).

An open reading frame encoding a protein having homology to MenA (a protein involved in menaquinone biosynthesis) was identified between nucleotides 20956-21834 of the insert from fosmid 101610 (SEQ ID NO: 1) and between nucleotides 37404-38282 of the insert from fosmid 60A5 (SEQ ID NO: 2). These open reading frames have been assigned SEQ ID NOs: 71 and 37 respectively in the accompanying sequence listing, while the polypeptides they encode have been assigned SEQ ID NOs: 72 and 38 respectively in the accompanying sequence listing.

An open reading frame encoding a protein having homology to the site specific DNA methyltranseferase proteins involved in restriction/modification was identified between nucleotides 26378-27454 of the insert from fosmid 101G10 (SEQ ID NO: 1) and between nucleotides 40563-41669 of the insert from fosmid 60A5 (SEQ ID NO: 2) on the strands complementary to the insert strands provided in SEQ ID NOs: 1 and 2. These open reading frames have been assigned SEQ ID NOs: 75 and 41 respectively in the accompanying sequence listing, while the polypeptides they encode have been assigned SEQ ID NOs: 76 and 42 respectively in the accompanying sequence listing.

An open reading frame encoding a protein having homology to the histone H1 DNA binding protein was identified between nucleotides 10625-1134 of the insert from fosmid 60A5 (SEQ ID NO: 2). This open reading frame has been assigned SEQ ID No: 5 in the accompanying sequence listing, while the polypeptide it encodes has been assigned SEQ ID No: 6 in the accompanying sequence listing.

An open reading frame encoding a protein having homology to lysyl tRNA synthetase was identified between nucleotides 13046-14620 of the insert from fosmid 60A5 (SEQ ID NO: 2). This open reading frame has been assigned

SEQ ID No: 9 in the accompanying sequence listing, while the polypeptide it encodes has been assigned SEQ ID No: 10 in the accompanying sequence listing.

A hypothetical open reading frame was identified between nucleotides 11478-13046 of the insert from fosmid 60A5 (SEQ ID NO: 2). This open reading frame has been assigned SEQ ID No: 7 in the accompanying sequence listing, while the polypeptide it encodes has been assigned SEQ ID No: 8 in the accompanying sequence listing.

An open reading frame encoding a protein having homology to peptidylprolyl cis/trans isomerase (a chaperone) was identified between nucleotides 20156-20434 of the insert from fosmid 101G10 (SEQ ID NO: 1) on the strand complementary to that provided in the sequence listing. This open reading frame has been assigned SEQ ID No: 67 in the accompanying sequence listing, while the polypeptide it encodes has been assigned SEQ ID No: 68 in the accompanying sequence listing.

An open reading frame encoding a protein having homology to glucose 1-dehydrogenase was identified between nucleotides 28065-29843 of the insert from fosmid 101G10 (SEQ ID NO: 1). This open reading frame has been assigned SEQ ID No: 79 in the accompanying sequence listing, while the polypeptide it encodes has been assigned SEQ ID No: 80 in the accompanying sequence listing.

A hypothetical open reading frame designated Hypothetical O1 was identified between nucleotides 1358-2290 of the insert from fosmid 101G10 (SEO ID NO: 1) and between nucleotides 17329-18213 of the insert from fosmid 60A5 (SEO ID NO: 2) on the strands complementary to the insert strands provided in SEO ID NOs: 1 and 2. These open reading frames have been assigned SEO ID NOs: 43 and 11 respectively in the accompanying sequence listing, while the polypeptides they encode have been assigned SEO ID NOs: 44 and 12 respectively in the accompanying sequence listing.

A hypothetical open reading frame designated Hypothetical O2 was identified between nucleotides 8961-9767 of the insert from fosmid 101G10 (SEO ID NO: 1) between nucleotides 24913-25728 of the insert from fosmid 60A5 (SEO ID NO: 2). These open reading frames have been assigned SEO ID NOs: 47 and 15 respectively in the accompanying sequence listing, while the polypeptides they encode have been assigned SEO ID NOs: 48 and 16 respectively in the accompanying sequence listing.

An open reading frame designated ORF 01 was identified between nucleotides 9772-10479 of the insert from fosmid 101G10 (SEQ ID NO: 1) and between nucleotides 25732-26427 of the insert from fosmid 60A5 (SEQ ID NO: 2) on the strands complementary to the insert strands provided in SEQ ID NOs: 1 and 2. These open reading frames have been assigned SEQ ID NOs: 49 and 17 respectively in the accompanying sequence listing, while the polypeptides they encode have been assigned SEQ ID NOs: 50 and 18 respectively in the accompanying sequence listing.

An open reading frame designated ORF 02 was identified between nucleotides 10545-10922 of the insert from fosmid 101G10 (SEQ ID NO: 1) and between nucleotides 26504-26881 of the insert from fosmid 60A5 (SEQ ID NO: 2). These open reading frames have been assigned SEQ ID NOs: 51 and 19 respectively in the accompanying sequence listing, while the polypeptides they encode have been assigned SEQ ID NOs: 52 and 20 respectively in the accompanying sequence listing.

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An open reading frame designated ORF 03 was identified between nucleotides 11382-11987 of the insert from fosmid 101G10 (SEQ ID NO: 1) and between nucleotides 27337-27936 of the insert from fosmid 60A5 (SEQ ID NO: 2) on the strands complementary to the insert strands provided in SEQ ID NOs: 1 and 2. These open reading frames have been assigned SEQ ID NOs: 53 and 21 respectively in the accompanying sequence listing, while the polypeptides they encode have been assigned SEQ ID NOs: 54 and 22 respectively in the accompanying sequence listing.

An open reading frame designated ORF 04 was identified between nucleotides 12916-13737 of the insert from fosmid 101G10 (SEQ ID NO: 1) and between nucleotides 28822-29631 of the insert from fosmid 60A5 (SEQ ID NO: 2) on the strands complementary to the insert strands provided in SEQ ID NOs: 1 and 2. These open reading frames have been assigned SEQ ID NOs: 55 and 23 respectively in the accompanying sequence listing, while the polypeptides they encode have been assigned SEQ ID NOs: 56 and 24 respectively in the accompanying sequence listing.

An open reading frame designated Hypothetical O3 was identified between nucleotides 20554-20955 of the insert from fosmid 101G10 (SEQ ID NO: 1) and between nucleotides 37002-37403 of the insert from fosmid 60A5 (SEQ ID NO: 2). These open reading frames have been assigned SEQ ID NOs: 69 and 35 respectively in the accompanying sequence listing, while the polypeptides they encode have been assigned SEQ ID NOs: 70 and 36 respectively in the accompanying sequence listing.

An open reading frame designated ORF 05 was identified between nucleotides 25151-26377 of the insert from fosmid 101G10 (SEQ ID NO: 1) and between nucleotides 39454-40572 of the insert from fosmid 60A5 (SEQ ID NO: 2). These open reading frames have been assigned SEQ ID NOs: 73 and 39 respectively in the accompanying sequence listing, while the polypeptides they encode have been assigned SEQ ID NOs: 74 and 40 respectively in the accompanying sequence listing.

An open reading frame encoding a protein with no homology to known proteins was identified between nucleotides 3-10421 of the insert from fosmid 60A5 (SEQ ID NO: 2). This open reading frame has been assigned SEQ ID No: 3 in the accompanying sequence listing, while the polypeptide it encodes has been assigned SEQ ID No: 4 in the accompanying sequence listing.

An open reading frame designated ORF06 was identified between nucleotides 27535-28002 of the insert from fosmid 101G10 (SEQ ID ND: 1). This open reading frame has been assigned SEQ ID No: 77 in the accompanying sequence listing, while the polypeptide it encodes has been assigned SEQ ID No: 78 in the accompanying sequence listing.

A gene coding for tRNA^{Tyr} was identified between nucleotides 12129-12251 of the insert from fosmid 101610 (SEQ ID NO: 1) and between nucleotides 28058-28180 of the insert from fosmid 60A5 (SEQ ID NO:2). This tRNA contains a 45 bp intron in the vicinity of the anticodon loop.

Table 1 shows the level of homology between the open reading frames in the inserts from fosmid 101G10 and fosmid 60A5 at the nucleic acid level. Table 1 also shows the level of homology at the amino acid level between

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the polypeptides encoded by the insert from fosmid 101G10 and fosmid 60A5. Nucleic acid homology was calculated using BLASTN with the default parameters. Amino acid homology was calculated using FASTA with the parameters. As shown in Table 1 and Fig. 1, the protein coding regions were highly similar in both nucleic acid and deduced amino acid sequences.

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Over the 28 kb common region in the 101610 and 60A5 inserts, the inserts shared > 99.2% identity in their ribosomal RNA genes, approximately 87.8% overall DNA identity, an average of 91.6% similarity in ORF amino acid sequence, and complete colinearity of protein encoding regions. As shown in Table 1, in protein coding regions the DNA identity of the two contigs ranged from 80.9% (triose phosphate isomerase) to 91.5% (Hypothetical 03). Within intergenic regions the identity dropped to 70 - 86 %, and small insertions or deletions were found frequently. The high similarity in coding regions and upstream sequences aided in the identification of genes, start codons, and putative transcriptional promoter motifs (see below). Genes appear as densely packed in *C. symbiosum* as they are in other sequenced archaeal genomes (Bult, C., et al. 1996. Complete genome sequence of the methanogenic archaeon, *Methanococcus jannaschii. Science* 273, 1058-1073, Klenk, H.P. et al. 1997. The complete genome sequence of the hyperthermophilic, sulphate-reducing archaeon *Archaeoglobus fulgidus. Nature* 390, 364-370; Smith, D. R., et al. 1997. Complete genome sequence of *Methanobacterium thermoautotrophicum* delta H: functional analysis and comparative genomics. *J. Bacteriol.* 179, 7135-7155).

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The ribosomal RNA operon of *Cenarchaeum symbiosum* is composed of the genes for the 16S and 23S rRNAs separated by a spacer of 131 bp. This organization is typical of crenarchaeotes, and differs from rRNA operons of euryarchaeotes, which usually contain 5S RNA and tRNA genes. (Garrett, R. A. *et al.* 1991. Archaeal rRNA operons. *TIBS* 16, 22-26). The large subunit rRNA genes are located between nucleotides 2680-5674 of SEO ID NO: 1 (fosmid 101610) and between nucleotides 18645-21639 of SEO ID NO: 2 (fosmid 60A5). The small subunit rRNA genes are located between nucleotides 5806-7278 of SEO ID NO: 1 (on the opposite strand from that shown in the Sequence Listing, as indicated in Figure 1) and between nucleotides 21771-23243 of SEO ID NO: 2. The large and small subunit rRNA genes in the two fosmids were 99.2% and 99.3% identical, respectively.

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As mentioned above, the sequences of the *Cenarchaeum symbiosum* derived inserts in fosmids 101610 and 60A5 had a high degree of homology but were not completely identical. The sequence of the insert in fosmid 101G10 was designated variant A, while the sequence of the insert in fosmid 60A5 was designated variant B. Such sequence differences could arise if the fosmid inserts were derived from two closely related but distinct strains of *Cenarchaeum symbiosum* or, alternatively, the sequence differences could be due to cloning or sequencing artifacts. To confirm that the fosmid inserts were in fact derived from two closely related strains, portions of the inserts in a plurality of different fosmids were sequenced to determine whether they were identical to either of the inserts in fosmids 101G10 and 60A5, as would be the case if there were in fact two closely related strains of *Cenarchaeum symbiosum*.

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In particular, the ribosomal RNA spacer regions of variant A and variant B contained 10 distinguishing signature nucleotides and the 16S rRNA genes of variant A and variant B contained two distinguishing nucleotides.

Example 5 provides the results of a PCR based analysis of the 16S rRNA gene and the 16S-23S spacer region in 13 different fosmid inserts.

Example 5

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PCR Based Analysis of Fosmid Inserts to Determine

Whether they Contain the Variant A or Variant B Sequences

Primers 21F and 459R-LSU (CTTTCCCTCACGGTA, SEQ ID NO: 116) were used to amplify the 16S-23S - spacer region from the fosmids. The amplification products were sequenced using primer SP23rev (CTA TTG CCG TCT TTA CACC, SEQ ID NO: 117).

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PCR reactions with two archaea-specific 16S rDNA primers (21F and 958R (DeLong, E. F. 1992. Archaea in coastal marine environments. *Proc. Natl. Acad. Sci.* 89, 5685-5689), one of which was biotinylated, were used to amplify a 950 base pair (bp) fragment from the fosmids. The PCR products were purified and sequenced as described in Preston, C. M. *et al.* 1996. A psychrophilic crenarchaeon inhabits a marine sponge: Cenarchaeum symbiosum gen. nov., sp. nov. *Proc. Natl. Acad. Sci.* USA 93, 6241-6246 with primer 519R 16S rDNA

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The results of this analysis are shown in Table 2. As shown in Table 2, in samples obtained from several unique rRNA operon-containing fosmids, a sequence identical to either variant A (101G10) or variant B (60A5) was present.

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The above methods may also be used to determine whether a biological sample contains variant A and/or variant B. In such procedures, nucleic acids are obtained from the biological sample, amplified using the above primers, and sequenced using the above oligonucleotide to determine whether the sample contains the variant A and/or the variant B sequence.

Similarly, the amplification reaction may be conducted using any primers which generate amplification products having sequences which differ between variant A and variant B. The amplification products may then be sequenced to determine whether they have the sequence of variant A and/or variant B. In some embodiment, the amplification reaction may be conducted under conditions in which the amplification primers specifically hybridize to one of the variants.

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RFLP analyses were also be used to assess whether the fosmids contained the sequence of variant A or variant B as described in Example 6 below.

Example 6

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RFLP Based Analysis of Fosmids to Determine Whether

They Contain the Variant A or Variant B Sequences

Primer set 21F (DeLong, E. F. 1992. Archaea in coastal marine environments. *Proc. Natl. Acad. Sci.* 89, 5685-5689) and 459R-LSU for the amplification of 2.2 kbp of the ribosomal operon, primer set GSAT810F (GAATCCGCC CCCGACTATCTT, SEQ ID NO: 118) and 16S37REV (CATGGCTTAGTATCAATC SEQ ID NO: 119) for the amplification of the 16S RNA-GSAT region (2.2 kbp) and primer set Cenpol357F (ACITACAACGGI GACGAYTTTGA

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SEQ ID NO: 120) and Cenpol735R (CACCCCGAARTAGTTYTTYTT SEQ ID NO: 121) for an internal DNA polymerase fragment (of 1134 bp) were used in PCR reactions with 5 ng of purified fosmids. The PCR products were cut with Taql and Hpall (16S-23S RNA), HaellI and Rsal (GSAT-16S RNA) or HaellI and Avail (polymerase) and analyzed on 2 % agarose gels.

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The results are shown in Table 2. If the pattern did not exactly match but closely resembled the RFLP of either type A or B, it was assigned as a lower case letter (a or b, Table 2), meaning that at least 3 out of 4 or 3 out of 5 bands created by restriction digest appear identical in size to the ones from either type A or B. As shown in Table 2, RFLP patterns of the 1150 bp fragment covering the 5'-end of the GSAT gene and 16S gene and the internal fragment of 1134 bp from the DNA polymerase gene revealed that all fosmids analyzed could again be assigned to either the A or B type, although slight variations were also detected (lower case letters in Table 2), suggesting that both variants exhibit further microheterogeneity which is detectable in protein coding and intergenic regions.

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The above methods may also be used to determine whether a biological sample contains variant A and/or variant B. In such procedures, nucleic acids are obtained from the biological sample, amplified using the above primers, and digested as described above to determine whether the sample contains the variant A and/or the variant B sequence. Similar analyses may also be performed using other portions of the sequences of SEQ ID NOs: 1 and 2 which are different from one another.

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To further confirm the existence of two closely related strains of *Cenarchaeum symbiosum*, biological samples were obtained from several individual sponges and analyzed to determine whether the samples contained variant A and/or variant B. Example 7 below provides the results of a PCR analysis of the *Cenarchaeum symbiosum* 16S rRNA genes in samples obtained from several individual sponges in different locations and at different times.

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Example 7

Analysis of Samples from Individual Sponges

The 16S rRNA genes of variant A and variant B differ at positions 175 and 183.7 (*E. coli* numbering). PCR reactions with two archaea-specific 16S rDNA primers (21F and 958R (DeLong, E. F. 1992. Archaea in coastal marine environments. *Proc. Natl. Acad. Sci.* 89, 5685-5689), one of which was biotinylated, were used to amplify a 950 base pair (bp) fragment from total nucleic acids derived from several different sponge individuals. The PCR products were purified and sequenced as described in Preston, C. M. *et al.* 1996. A psychrophilic crenarchaeon inhabits a marine sponge: Cenarchaeum symbiosum gen. nov., sp. nov. *Proc. Natl. Acad. Sci.* USA 93, 6241-6248 with primer

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519R.

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The amplification products were sequenced to determine whether they corresponded to variant A and/or variant B. The results are shown in Table 3. As shown in Table 3, in 15 out of 16 cases U/C ambiguities were found at the signature positions, indicating the presence of both variants in samples obtained from a single sponge (Table 3). Only one sponge (S4) yielded an unambiguous sequence identical to variant A, but variant B was detected in this individual by another criterion (see below).

Hybridization analyses were also used to determine whether individual sponges harbored variant A and/or variant B. The results of these analyses are provided in Example 8 below.

Example 8

<u>Hybridization Based Analysis of Samples Obtained from Axinella Mexicana</u> to Determine Whether the Samples Contain Variant A and/or Variant B

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Two oligonucleotides specific for each variant type were designed from the 23S rDNA gene sequences of fosmids 101G10 and 60A5. The probes differed in 3 positions and have the sequences ACACTTCAACTATTTCCTG (SEQ ID NO: 122 variant A) and ACACTTTGACTATTTCGTG (SEQ ID NO: 123, variant B). Nucleic acid samples from individual sponges (300 ng) and controls (fosmids 101G10 and 60A5, 50 ng each) were denatured, bound to nylon membranes (Hybond-N, Amersham), hybridized with the labeled probes (Massana, R. et al. 1997. Vertical distribution and phylogenetic characterization of marine planktonic Archaea in the Santa Barbara Channel. *Appl. Env. Microb.* 63, 50-56) and washed at 41.5 °C. Hybridization was analyzed by autoradiography.

The results are provided in Table 3. In the samples from the majority of host sponges examined, the presence of both 23S rRNA variants was observed, confirming that the specific association of *C. symbiosum* with its host typically involves the presence of both variants.

The data provide strong evidence that these genomic clones are derived from two very closely related, but distinct strains, as opposed to representing two ribosomal RNA operon regions originating from the same organism. This conclusion is consistent with the observation that all crenarchaeota characterized to date contain only one ribosomal RNA operon (Garrett, R. A. et al. 1991. Archaeal rRNA operons. *TIBS* 16, 22-26).

The high conservation between the inserts in fosmid 101G10 and fosmid 60A5 was not entirely confined to coding regions but also extended into adjacent upstream sequences. Due to this upstream similarity, and also because the average G+C content of the sequences was relatively high, it was possible to readily identify prospective transcriptional (A+T rich) promoter elements. A motif corresponding to the consensus of the archaeal TATA-box-like element (C/T-T-A-T/A-A) (Hain, J. et al. 1992. Elements of an archaeal promoter defined by mutational analysis. Nucl. Acids. Res. 20, 5423-5428) was identified upstream of nearly all genes (Fig. 2). The exceptions were the genes encoding MenA and DNA polymerase which are located immediately downstream of other ORFs and may therefore be transcribed as polycistronic mRNAs. In vivo and in vitro studies in other archaea have shown that initiation of transcription occurs consistently 24 to 28 bp downstream from the central T of this motif (Hain, J et al. 1992. Elements of an archaeal promoter defined by mutational analysis. Nucl. Acids. Res. 20, 5423-5428; Palmer, J. R. and Daniels, C.J. 1995. In vivo definition of an archaeal promoter. J. Bacteriol. 177 1844-1849). For twelve of the protein encoding genes, the promoter element was found 25 to 30 bp upstream of the ORF (Fig. 2), suggesting that transcriptional initiation occurs in close proximity to, or directly at, the translational start codon.

A similar observation has been made for 30 of the predicted 100 strong and medium promoters from 156 kbp sequence of Sulfolobus solfataricus (Sensen, C. W. et al. 1996. Organizational characteristics and information

content of an archaeal genome: 156 kb of sequence from Sulfolobus solfataricus P2. Molec. Microb. 22, 175-191). Transcription initiation at, or in close proximity to, the translational start codons has been mapped for some genes in Halobacterium salinarium (Brown, J.W. et al. 1989. Gene structure, organization, and expression in archaebacteria. CRC Crit. Rev. Microb. 16, 287-337) and S. solfataricus (Klenk, H.P., et al. 1993. Nucleotide sequence, transcription and phylogeny of the gene encoding the superoxide dismutase of Sulfolobus acidocaldarius. Biochim. Biophys. Acta 1174 95-98), and alternative mechanisms for initial mRNA-ribosome contact in Archaea have been hypothesized (Brown, J.W. et al. 1989. Gene structure, organization, and expression in archaebacteria. CRC Crit. Rev. Microb. 16, 287-337).

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The promoters listed in Figure 2, or fragments thereof, may be used in expression vectors or expression systems. In one embodiment, the promoters listed in Figure 2 may be operably linked to coding regions and introduced into archaebacteria, and in particular *Cenarchaeum symbiosum*, to express the encoded gene product in the archaebacterial cells.

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Alternatively, the promoters listed in Figure 2 may be operably linked to coding regions and introduced into host cells which are not normally capable of directing transcription from archaebacterial promoters. In addition, genes encoding the proteins required for transcription from these promoters are also introduced into the host cells. The genes encoding these transcription factors may be on the same vector as the promoter from *Cenarchaeum symbiosum* or on a different vector. In some embodiments, the genes encoding these transcription factors are linked to an inducible promoter. Expression of the transcription factors is induced when it is desired to express the proteins which are operably linked to the promoter from *Cenarchaeum symbiosum*.

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Although this invention has been described in terms of certain preferred embodiments, other embodiments which will be apparent to those of ordinary skill in the art in view of the disclosure herein are also within the scope of this invention. Accordingly, the scope of the invention is intended to be defined only by reference to the appended claims.

Table 1

Comparison of Overlapping Coding Sequences from Fosmid 101G10

and Fosmid 60A5

Gene	Functional	% Id	entity
Name ¹	Category	Nucleotide	Amino Acid
Hypothetical 01	unknown	81.4	76.6
238	translation	99.16	
16S	translation	99.3	
GSAT	heme biosynthesis	83.2	83.8
Hypothetical 02	unknown	83.4	81.4
ORF 01	unknown	83.3	85.7
ORF 02	unknown	89.9	95.2
ORF 03	unknown	87.9	86.7
tRNA ^{tyr}	translation	99.2	
ORF 04	unknown	87.8	88.1
TIM	glycolysis	80.9	83.3
ТВР	transcription	83.4	86.3
DNA polymerase	replication/repair	89.0	93.9
dCMP deaminase	pyrimidine synthesis	85.7	89.8
RNA helicase (ATP	translation	86.1	92.2
dependent)			
PPI	chaperone	88.4	92.5
Hypothetical 03	unknown	91.5	92.4
MenA	menaquinone biosynthesis	86	89.4
ORF 05	unknown	87.5	90.6
Methylase	restriction/modification	86.4	87.5

¹ Hypothetical: open reading frame (ORF) with similarity to proteins of unknown function from the databases.

ORF - open reading frame identified by similarity between both fosmids, including upstream promoter sequence;

GSAT - glutamate semialdehyde aminotransferase; TIM - triose-phosphate isomerase; TBP - TATA box-binding protein; PPI - peptidylprolyl cis/trens isomerase.

Table 2

Analysis of Polymorphism at Four Distinct Loci in Different Fosmids

Fosmid	16S RNA"	16S-23S	16S-GSAT*3		DNA	Pol ⁻³
		spacer*2	Haelll	Rsal	Haelil	Avall
101G10	A	Α	A,	A	A	Α
60A5	В	В	В	B	В	В
15A5	В	В	••	••	b	b
43H4	A		••	••	A	A
60H6	A	A	••	••	a/b	В
69H2	A		••	••	Α	A
87F4	В				b	a/b
C1H5	A	Α	. А	Α		
C4H1	A	Α	Α	Α		
C4H9	A	A	A	Α	A	В
C7D4	A	Α	Α	Α	Α	A
C8B8	В	В	В	В	В	b
C15A3	A	A	Α	Α		
C17D2	8	••	b	В	В	b
C20B5	A	Α	a	a/b		

^{*1:} partial sequence (101G10 through 87F4) or RFLP analysis (C1H5 through C20B5).

The first seven fosmids were isolated from a first library, the last 8 fosmids (prefix C) are from a second library.

^{*2:} partial sequence.

^{*3:} RFLP analysis of PCR products; A/B: identical pattern to either 101G10 (-A) or 60A5 (-B); a,b: similar pattern to either A or B (see materials and methods). Fosmids C1H5, C4H1, C15A3 and C20B5 did not yield PCR products with polymerase-specific primers.

^{-- =} not determined.

Table 3

Detection of *C. symbiosium* Variants in Natural Populations of *A. mexicana*

A. mexicana Individual or Isolated DNA Source*		on in 16S ositions**		n 23S rRNA lization
10010100 51111 000.00	175	183.7	Variant Type A	Variant Type E
fosmid 101G10 from s12	U	U	+	•
fosmid 60A5 from s12	C	C	•	+
s12	Y	Y	+	+
s1	•••	•••	+	+
s 2	***		+	+
s 3	Y	Y	+	+
34	U	U	+	w
s 5	Y	· Y	***	•••
s6	Y	Y	+	+
s7	•••	•••	+	w
s 8	Y	Y	+	+
s 9	Y	Y	+	w
s 10	***	•••	+	+
s 11	Y	Y	+	+
s13	***	•••	+	+
s14	•••	•••	+	w
s 16	•••	•••	+	+
s17	***	•••	•	w
s18	Y	Y	•	w
s19	•••	•••	+	+
s20		•••	+	+
s21		***	+	+
s22	***	•••	+	+
s23	•••	***	+	+
s24	•••	•	+	+
s25	. •••		+	+
s26	•••	•••	+	+
s27	•••	•••	+	+
s 28	•••		+	+
s29	***	***	+	+
s30	***	•••	+	+
hs 1	•••	***	+	+
hs2	•••	***	+	+
hs3	Y	Y	+	w
hs4	Y	Y	+	w
hs5	Y	Y	+	+
hh1	•••	•••	w	w
hh2	Y	Y	+	+
hh3	Ý	Y	+	+
Aq1	Ÿ	Y	***	•••
Aq2	Ý	Y	***	•••
Aq3	•		+	+

^{*}s = Naples Reef; hs = Haskle; hh = Hermit Hole; Aq = captive sponge.

^{**}Y = direct sequence of PCR product yields C and U at the same position.

^{··· =} not determined; w = weakly positive.

WHAT IS CLAIMED IS:

1. An isolated, purified, or enriched nucleic acid comprising a sequence selected from the group consisting of SEQ ID NO: 1 and SEQ ID NO: 2, the sequences complementary to SEQ ID NO: 1 and SEQ ID NO: 2, fragments comprising at least 10 consecutive nucleotides of SEQ ID NO: 1 and SEQ ID NO: 2, and fragments comprising at least 10 consecutive nucleotides of the sequences complementary to SEQ ID NO: 1 and SEQ ID NO: 2.

- 2. An isolated, purified, or enriched nucleic acid capable of hybridizing to the nucleic acid of Claim 1 under conditions of high stringency.
- An isolated, purified, or enriched nucleic acid capable of hybridizing to the nucleic acid of Claim 1 under conditions of moderate stringency.
- 4. An isolated, purified, or enriched nucleic acid capable of hybridizing to the nucleic acid of Claim 1 under conditions of low stringency.
- 5. An isolated, purified, or enriched nucleic acid having at least 70% homology to the nucleic acid of Claim 1 as determined by analysis with BLASTN version 2.0 with the default parameters.
- 6. An isolated, purified, or enriched nucleic acid having at least 99% homology to the nucleic acid of Claim 1 as determined by analysis with BLASTN version 2.0 with the default parameters.
- 7. An isolated, purified, or enriched nucleic acid comprising a sequence selected from the group consisting of SEQ ID NOs: 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79 and the sequences complementary thereto.
- 8. An isolated, purified, or enriched nucleic acid capable of hybridizing to the nucleic acid of Claim 7 under conditions of high stringency.
- An isolated, purified, or enriched nucleic acid capable of hybridizing to the nucleic acid of Claim 7 under conditions of moderate stringency.
- 10. An isolated, purified, or enriched nucleic acid capable of hybridizing to the nucleic acid of Claim 7 under conditions of low stringency.
- 11. An isolated, purified, or enriched nucleic acid having at least 70% homology to the nucleic acid of Claim 7 as determined by analysis with BLASTN version 2.0 with the default parameters.
- 12. An isolated, purified, or enriched nucleic acid having at least 99% homology to the nucleic acid of Claim 7 as determined by analysis with BLASTN version 2.0 with the default parameters.
- 13. An isolated, purified, or enriched nucleic acid comprising at least 10 consecutive bases of a sequence selected from the group consisting of SEQ ID NOs: 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79 and the sequences complementary thereto.
- 14. An isolated, purified, or enriched nucleic acid having at least 70% homology to the nucleic acid of Claim 13 as determined by analysis with BLASTN version 2.0 with the default parameters.

15. An isolated, purified, or enriched nucleic acid comprising a sequence selected from the group consisting of SEQ ID NOs: 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73, 77 and the sequences complementary thereto.

- 16. An isolated, purified, or enriched nucleic acid capable of hybridizing to the nucleic acid of Claim 15 under conditions of high stringency.
- 17. An isolated, purified, or enriched nucleic acid capable of hybridizing to the nucleic acid of Claim 15 under conditions of moderate stringency.
- 18. An isolated, purified, or enriched nucleic acid capable of hybridizing to the nucleic acid of Claim 15 under conditions of low stringency.
- 19. An isolated, purified, or enriched nucleic acid having at least 70% homology to the nucleic acid of Claim 15 as determined by analysis with BLASTN version 2.0 with the default parameters.
- 20. An isolated, purified, or enriched nucleic acid having at least 99% homology to the nucleic acid of Claim 15 as determined by analysis with BLASTN version 2.0 with the default parameters.
- 21. An isolated, purified, or enriched nucleic acid comprising at least 10 consecutive bases of a sequence selected from the group consisting of SEQ ID NOs: 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73, 77 and the sequences complementary thereto.
- 22. An isolated, purified, or enriched nucleic acid having at least 70% homology to the nucleic acid of Claim 21 as determined by analysis with BLASTN version 2.0 with the default parameters.
- 23. An isolated, purified, or enriched nucleic acid having at least 99% homology to the nucleic acid of Claim 21 as determined by analysis with BLASTN version 2.0 with the default parameters.
- An isolated, purified, or enriched nucleic acid encoding a polypeptide having a sequence selected from the group consisting of SEQ ID NOs: 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, and 80.
- 25. An isolated, purified, or enriched nucleic acid encoding a polypeptide comprising at least 10 consecutive amino acids of a polypeptide having a sequence selected from the group consisting of SEQ ID NOs: 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, and 80.
- An isolated, purified, or enriched nucleic acid encoding a polypeptide having a sequence selected from the group consisting of SEQ ID NOs: 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78.
- 27. An isolated, purified, or enriched nucleic acid encoding a polypeptide comprising at least 10 consecutive amino acids of a polypeptide having a sequence selected from the group consisting of SEO ID NOs: 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78.
- 28. An isolated or purified polypeptide comprising a sequence selected from the group consisting of SEQ ID NOs: 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, and 80.

29. An isolated or purified polypeptide comprising at least 10 consecutive amino acids of the polypeptides of Claim 28.

- 30. An isolated or purified polypeptide having at least 70% homology to the polypeptide of Claim 28 as determined by analysis with FASTA version 3.0t78 with the default parameters.
- 31. An isolated or purified polypeptide having at least 99% homology to the polypeptide of Claim 28 as determined by analysis with FASTA version 3.0t78 with the default parameters.
- 32. An isolated or purified polypeptide having at least 70% homology to the polypeptide of Claim 29 as determined by analysis with FASTA version 3.0t78 with the default parameters.
- 33. An isolated or purified polypeptide having at least 99% homology to the polypeptide of Claim 29 as determined by analysis with FASTA version 3.0t78 with the default parameters.
- 34. An isolated or purified polypeptide comprising a sequence selected from the group consisting of SEO ID NOs: 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78.
- 35. An isolated or purified polypeptide comprising at least 10 consecutive amino acids of the polypeptides of Claim 34.
- 36. An isolated or purified polypeptide having at least 70% homology to the polypeptides of Claim 34 as determined by analysis with FASTA version 3.0t78 with the default parameters.
- 37. An isolated or purified polypeptide having at least 99% homology to the polypeptides of Claim 34 as determined by analysis with FASTA version 3.0t78 with the default parameters.
- 38. An isolated or purified polypeptide having at least 70% homology to the polypeptides of Claim 35 as determined by analysis with FASTA version 3.0t78 with the default parameters.
- 39. An isolated or purified polypeptide having at least 99% homology to the polypeptides of Claim 35 as determined by analysis with FASTA version 3.0t78 with the default parameters.
- 40. An isolated or purified antibody capable of specifically binding to a polypeptide comprising a sequence selected from the group consisting of SEQ ID NOs: 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, and 80.
- An isolated or purified antibody capable of specifically binding to a polypeptide comprising at least 10 consecutive amino acids of one of the polypeptides of SEQ ID NOs: 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, and 80.
- 42. An isolated or purified antibody capable of specifically binding to a polypeptide having a sequence selected from the group consisting of SEQ ID NDs: 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78.
- An isolated or purified antibody capable of specifically binding to a polypeptide comprising at least 10 consecutive amino acids of one of the polypeptides of SEO ID NOs: 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78.

A method of making a polypeptide having a sequence selected from the group consisting of SEQ ID NOs: 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, and 80 comprising introducing a nucleic acid encoding said polypeptide, said nucleic acid being operably linked to a promoter, into a host cell.

- 45. A method of making a polypeptide comprising at least 10 amino acids of a sequence selected from the group consisting of the sequences of SEO ID NOs: 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, and 80 comprising introducing a nucleic acid encoding said polypeptide, said nucleic acid being operably linked to a promoter, into a host cell.
- 46. A method of making a polypeptide having a sequence selected from the group consisting of SEQ ID NOs: 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78 comprising introducing a nucleic acid encoding said polypeptide, said nucleic acid being operably linked to a promoter, into a host cell.
- 47. A method of making a polypeptide comprising at least 10 amino acids of a sequence selected from the group consisting of the sequences of SEQ ID NOs: 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78 comprising introducing a nucleic acid encoding said polypeptide, said nucleic acid being operably linked to a promoter, into a host cell.
 - 48. A method of generating a variant comprising:

obtaining a nucleic acid comprising a sequence selected from the group consisting of SEQ ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77, the sequences complementary to the sequences of SEQ ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77, fragments comprising at least 30 consecutive nucleotides of SEQ ID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77, and fragments comprising at least 30 consecutive nucleotides of the sequences complementary to SEQ ID NOS. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77, and fragments comprising at least 30 consecutive nucleotides of the sequences complementary to SEQ ID NOS. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77; and

changing one or more nucleotides in said sequence to another nucleotide, deleting one or more nucleotides in said sequence, or adding one or more nucleotides to said sequence.

- 49. The method of Claim 48, further comprising the step of testing the enzymatic properties of a translation product of said variant.
- A computer readable medium having stored thereon a sequence selected from the group consisting of a nucleic acid code of SEQID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 and a polypeptide code of SEQ ID NOs. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78.
- A computer system comprising a processor and a data storage device wherein said data storage device has stored thereon a sequence selected from the group consisting of a nucleic acid code of SEOID NOs. 1, 2, 5, 9, 13, 25,

27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 and a polypeptide code of SEQ ID NOs. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78.

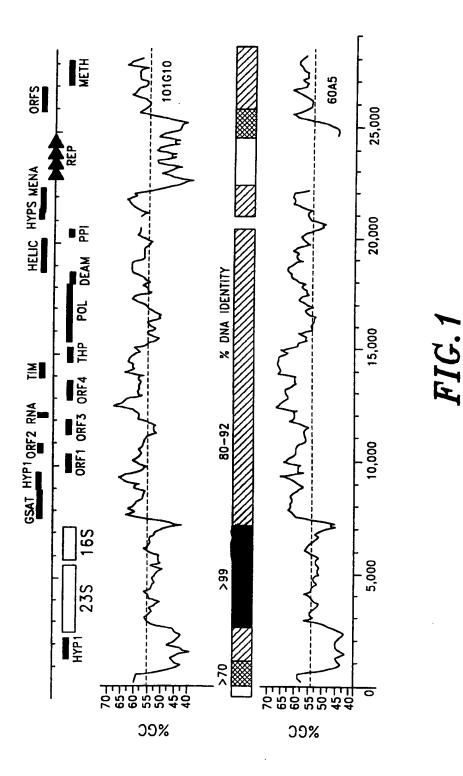
- The computer system of Claim 51 further comprising a sequence comparer and a data storage device having reference sequences stored thereon.
- 53 The computer system of Claim 52 wherein said sequence comparer comprises a computer program which indicates polymorphisms.
- The computer system of Claim 51 further comprising an identifier which identifies features in said sequence.
- A method for comparing a first sequence to a reference sequence wherein said first sequence is selected from the group consisting of a nucleic acid code of SEQID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 and a polypeptide code of SEQ ID NOs. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78 comprising the steps of:

reading said first sequence and said reference sequence through use of a computer program which compares sequences; and

determining differences between said first sequence and said reference sequence with said computer program.

- The method of Claim 55, wherein said step of determining differences between the first sequence and the reference sequence comprises identifying polymorphisms.
- A method for identifying a feature in a sequence selected from the group consisting of a nucleic acid code of SEQID NOs. 1, 2, 5, 9, 13, 25, 27, 29, 31, 33, 37, 41, 45, 57, 59, 61, 63, 65, 67, 71, 75, 79, 3, 7, 11, 15, 17, 19, 21, 23, 35, 39, 43, 47, 49, 51, 53, 55, 69, 73 and 77 and a polypeptide code of SEQ ID NOs. 6, 10, 14, 26, 28, 30, 32, 34, 38, 42, 46, 58, 60, 62, 64, 66, 68, 72, 76, 80, 4, 8, 12, 16, 18, 20, 22, 24, 36, 40, 44, 48, 50, 52, 54, 56, 70, 74, and 78 comprising the steps of:

reading said sequence through the use of a computer program which identifies features in sequences; and identifying features in said sequence with said computer program.



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84		B GGAAACTTTG	ATTATA CGGG CGTACATICC	CGGGGCCCAT G	
85	ORF C2		AATAAT AGCC TGCCGTCTGT	AACGGCCGTA TG	27
86		B ACGCCAAGGT	AATAAT AGCC TGCCGTCCGT	ACCIGCCGIA IG	
87	ORF 03	CAT	GATATT AACC GGTTCCGCGG	ATCCCATGCA TG	27
88		B CATGGAACTA	GATAAT AACC GGTCCCGCGG	GTACAATGCA TG	
68	PPI		GITAIA GCAG GGIATGGAAT		28
06		AAG		AGCAGCGCAC ATG	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
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95		ATC	ATTAAA TTAC GGGGGGTACA	ACCIGCIGCC GIG	!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!!
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94		ACT		TCGTCCGCGC ATC	
ر د د	deaminase	G	CATAAT ATGC CGGGCGGTGG	CACCAIGGCC GITO	29
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76	RNA halic	TGT	ACAA	CAGGGCCGCG CGTG	29
80		990	CATAAA ACAA CAGGCCGCGG	CAGGGCG.CG CGTG	
თ	ORF 06	A : .		GCGCGIATCA CATG	29
100				GCGCGGACCA CATG	
101	tRNA-tyr	90		CACGGATCGT CCCA	29
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104			GTTAAA ATAG AGTGCGGCCG	GGCACCGGAT CAATG	ŧ
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106		ပ္ပ	AATAAA TACG CGC.GGGGCC	GCGGTGC GATCGCCCGT	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
107	Hypoth 01	ATT	CATAAA TGCC TAGTTACGCA		TCGACTAATG 49
108		ACT		GAAATATCAA ACAAAQTACT	•
109	04F C1	ACG	ATTAIT ACCT IGCCIIGCGI	TGTA //G CGGGGTGCGG	CAGGGGATG 52
110		ACG	ATTAIT ACCT IGCCGIGIG.)
111	Methylase		TITAAG TCGG CGCCGGGGCA	GCCG.//G ATGTGGGGCA	GGCAACATG 104
112			TITAAG ACGG CGCGGGTGCC		1
113	168 RNA	TCG		CCGATCCGAT CGTACGTGAC	GC. ' ' . AAT 220
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Archaeal	l promoter		7		
consensas	15		yttama K	٠	

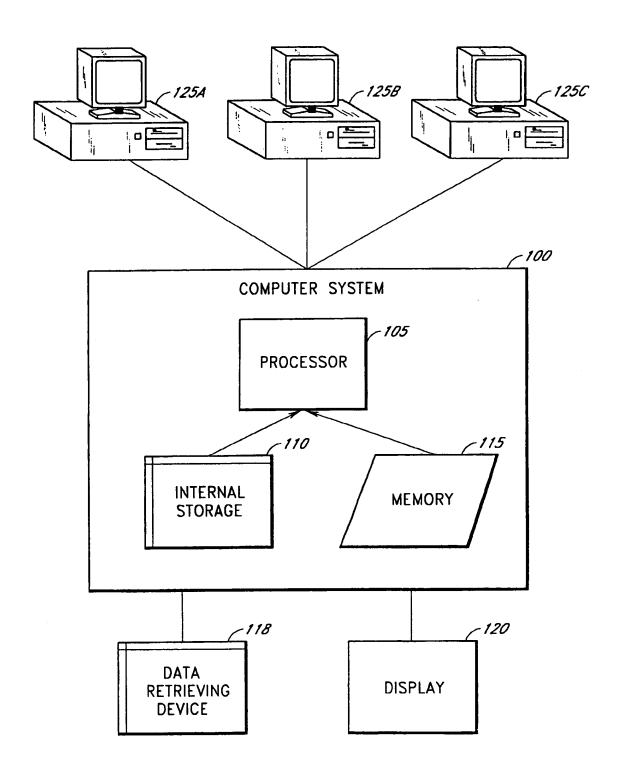


FIG.3

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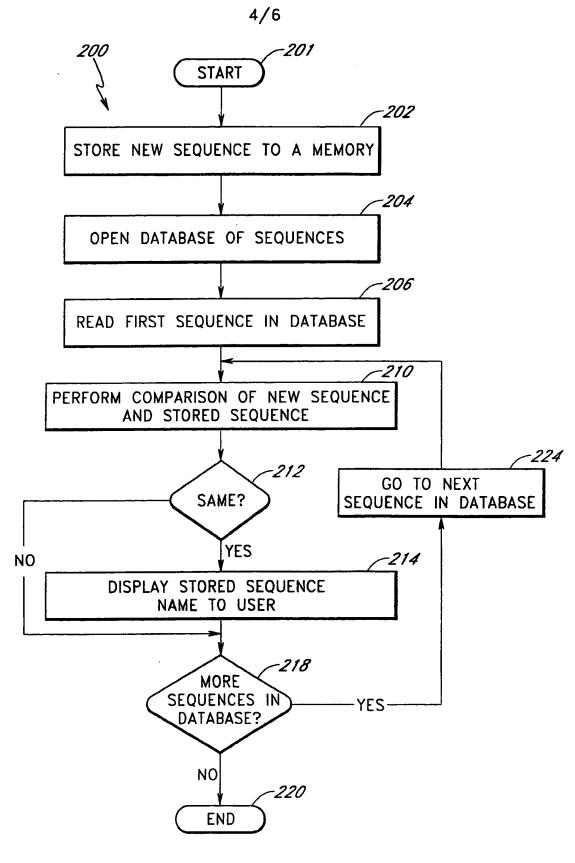
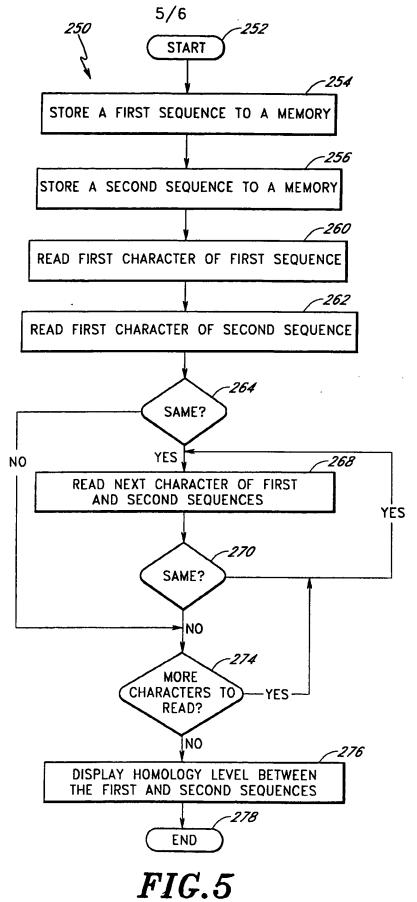


FIG.4

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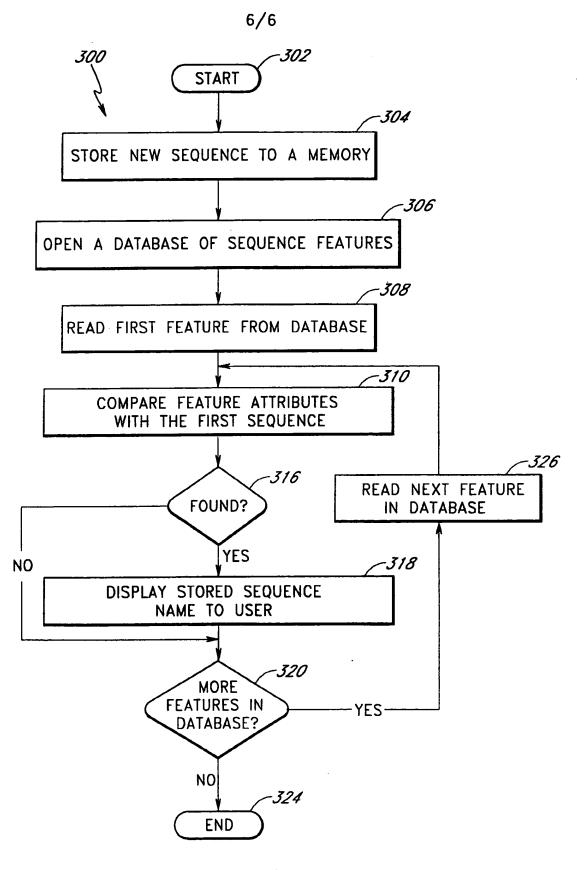


FIG.6

SUBSTITUTE SHEET (RULE 26)

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-24-

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Asp Asp Gly Arg Tyr Met Tyr Ala Ile Gly Arg Asp Leu Leu Thr Va	
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	.c 144
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	ac 144 eu
tac egg tat aca atg aac eeg eec cat gac ata gee teg gee geg et Tyr Arg Tyr Thr Met Asn Pro Pro His Asp Ile Ala Ser Ala Ala Le	.c 144 eu
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tac cgg tat aca atg aac ccg ccc cat gac ata gcc tcg gcc gcg ctc Tyr Arg Tyr Thr Met Asn Pro Pro His Asp Ile Ala Ser Ala Ala Le 35 40 45 ggt gcg cag tca ttt tct ctg cct ggc ggc atc agc ccc gcc ccc gg Gly Ala Gln Ser Phe Ser Leu Pro Gly Gly Ile Ser Pro Ala Pro Gl 50 55 60 gcg ccg acc ggc ctt gac atc tcg gat gac ggc cgc cac ctg tac gt Ala Pro Thr Gly Leu Asp Ile Ser Asp Asp Gly Arg His Leu Tyr Va 65 70 75 8	192 Y 240 11 10 288

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•	gtt Val	gcc Ala	gcg Ala 115	ccc Pro	cgc Arg	ggc Gly	gta Val	tac Tyr 120	gtg Val	gcg Ala	ccg Pro	ggc Gly	ggc Gly 125	agc Ser	ctc Leu	atg Met		384
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9	gcg Ala	ggc Gly	acg Thr 195	cac His	cag Gln	ata Ile	cag Gln	gag Glu 200	gca Ala	gcc Ala	gca Ala	Gly 333	ccg Pro 205	cgg Arg	ctg Leu	ctc Leu	•	624
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								cgg Arg									9	960
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	ggc Gly 610															1872
	agg Arg															1920
	ctg Leu															1968
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	atg Met															2256
	ccg Pro															2304
	gac Asp 770			_												2352
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	gat Asp	_									_			_	-	2688
	ggc															2736
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	gtg Val 930															2832
	ccg Pro															2880
	gag Glu														-	2928
	ctg Leu	Thr														2976
	gac Asp		Pro			Arg		Tyr					Asn			3024
	gac Asp 1010	Ile	_		Ala		Pro				_	Ile			-	3072

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1485

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	Tyr			-		Pro					Ser				ata Ile 1520	4560
	_		tcg Ser	_	Pro		_	_	_	Pro			_	_	Phe	4608
_		-	999 Gly 154	Arg		_		_	Ser					Ile	_	4656
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		Ile	ccc Pro				Gly					Arg				4752
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			cgc Arg					Phe		-			Asn	_	-	4944
		Ser	ggc Gly				Ser					Gly			_	4992
	Gly		gly ggg	_		Gly					Ser					5040
			acc Thr		Pro					Leu					Gly	5088
			gtt Val 1700	Asp	_	-			Glu					Leu		5136
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				Ile					gtt Val					Leu		6096
			Asp					Phe	ata Ile				Ala			6144
		Arg					Asp		ttc Phe			Glu				6192
	Gln					Leu			cca Pro		Ala					6240
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				qaA					ttt Phe					Pro		6336
	-	_	Leu	_				Leu	gag Glu				Val			6384
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	Phe	_	_			Ser	_		ggc Gly		Leu				_	6480
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_		Leu	_	_		_	Val					Ile		ttc Phe		6912
	Asp					Phe					Asp			cac His		6960
	~		•	_	Asn	_			_	Ile	_		_	ata Ile 2335	Leu	7008
_			_	Ser		-	_	_	Asn		_	_) GJÀ aaa	_	7056
			Glu					Ala					Gly	cgt Arg		7104
	-	Thr					Leu					Leu		ggc		7152
	Ser	_	-		_	Ala					Tyr			gag Glu		7200
					Asp					Asp				cgc Arg 2415	Met	7248

+35-

				Val					Arg				_	Leu	tcg Ser	7296
_		_	Thr	_		_	-	His			_	acg Thr 244	Asp	_	ctg Leu	7344
		Asp				_	Gly		_			gat Asp 0		-	J	7392
	Phe	_			_	Arg	_			_	Arg	cag Gln				7440
					Ala					Leu		gac Asp			Leu	7488
	_		_	Val	_		_	_	Ser			cgg Arg		Thr		7536
-		_	Lys	_			_	Gly	_		_	gcc Ala 2525	Met			7584
		Ser					Tyr					gcg Ala	_		_	7632
	Val					Gly					Ala	ggt Gly	_		-	7680
					Ser					Asp		tcg Ser			Gly	7728
				Val					Leu	-		agg Arg		Phe	_	7776
			lyr			_	-	Ala				ggc Gly 2605	Ser			7824
		Arg					Leu					cgg Arg				7872
	Phe					Ser					Leu	aaa Lys				7920
aac	gca	caa	cct	gtc	ggc	aac	ata	acc	cat	gcc	gat	acg	cgc	gcc	999	7968

									-36	-						
Asn	Ala	Gln	Pro	Val 264	_	Asn	Ile	Thr	His 265		Asp	Thr	Arg	Ala 265	Gly 5	
				Ala					Gly					Thr	cgc Arg	8016
			Leu					Val					Val		att Ile	8064
		Phe					Gly					Arg			tat Tyr	8112
						Leu					Asn				aat Asn 2720	8160
	gtt Val				Val					Glu					Ser	8208
	cat His	_		Pro					Ile					Pro		8256
	aca Thr		Ala					His					Ser			8304
	tcc Ser 2770	Gly					Ser					Ser				8352
	gag Glu					Ala					Gly					8400
	gga Gly				Ser					Asp					Asp	8448
	atg Met			Thr					Val					Pro		8496
	ggg Gly		Ala					Ser					Ala			8544
	gcc Ala 2850	Asp					Asp					Thr				8592
	gtg Val		_	_	_	Pro	-	_			Ala					8640

		_			Ala		_	_	-	Asp			_	_	gac Asp 5	8688
				Thr					Val		gac Asp	-	_	Pro	-	8736
			Ala					Ser			Gly aaa		Ala		_	8784
		Asp					Asp				gat Asp 294	Thr				8832
	Thr					Pro					gaa Glu 5					8880
					Ser	-				Gly	ggc Gly	_		_	Ser	8928
				His					Glu		cgc Arg			Gly		8976
			Gly					Ile			aag Lys		Ser			9024
`\		Ala					Arg				gca Ala 3020	Met				9072
	Val				_	Arg				_	gcg Ala		_	-		9120
					Ser					Pro	agg Arg				Met	9168
				Val					Ser		gcc Ala			Ala		9216
			Gly			Pro		Phe			gcg Ala		Arg			9264
		Gly									aca Thr 3100	Val				9312
cac	agt	ctg	gcc	cgg	gcc	gca	tac	ata	tcc	gaa	ggc	gat	tcc	ccg	aca	9360

-38-

									-							
His 310		Leu	Ala	Arg	Ala 311		Ser	Ile	Ser	Glu 311	-	Asp	Ser	Pro	Thr 3120	
				_	Arg		_		-	Gly	_		_		gtg Val 5	9408
				Val					Leu					Leu	cag Gln	9456
			Ser					Asp				ata Ile 316	Asp		tcg Ser	9504
		Ser					Pro					gtg Val O				9552
	Gly					Gly		_		_	Gly	ctt Leu	_	_		9600
					Ile					Arg		gac Asp			Leu	9648
				Gly					Ala			Gly		Asp		9696
			Pro					Glu				aac Asn 3245	Ile			9744
		Val	_			_	Pro					tcg Ser		_		9792
	Asn					Leu					Cys	ggc Gly				9840
					Tyr					Leu		ata Ile			Asp	9888
				Val					Ala			ggc Gly		Val		9936
		-	Gly			_		Thr		_	_	tcg Ser 3325	Leu	_	_	9984
		Gly			_	-	Gln			_		aaa Lys				10032

-39-

ttg att ttg gac gcc gct gaa aac a Leu Ile Leu Asp Ala Ala Glu Asn A 3345 3350	
ccc aag ccc gtg gag gat cca tcg c Pro Lys Pro Val Glu Asp Pro Ser F 3365	
cag atg gat ccg gag ccc gtg gag t Gln Met Asp Pro Glu Pro Val Glu S 3380	
gag ccc gtg gag gat ctg gaa cct g Glu Pro Val Glu Asp Leu Glu Pro V 3395 3400	
atg gac ccc gag ccc gtg gag gat c Met Asp Pro Glu Pro Val Glu Asp L 3410 3415	
ccc gtg cag gga tcc ccg ccc gtg c Pro Val Gln Gly Ser Pro Pro Val G 3425 3430	
tca ggc ata gca tac acg cta tgg c Ser Gly Ile Ala Tyr Thr Leu Trp G 3445	
gcc ctg ggt ctt gcc gac ccg gat g Ala Leu Gly Leu Ala Asp Pro Asp V 3460 3	
tga *	10419
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<400> 4	
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1 5 Asp Asp Gly Arg Tyr Met Tyr Ala II 20 2:	
Tyr Arg Tyr Thr Met Asn Pro Pro H	
35 40 Gly Ala Gln Ser Phe Ser Leu Pro G	· ·
50 55 Ala Pro Thr Gly Leu Asp Ile Ser As	•
65 70 Pro Asp Glu Asn Gly Val Val Tyr A	
85 Arg Leu Asp Gly Gly Thr Phe Gly Se	
100 10 Val Ala Ala Bro Arg Gly Val Tyr Va	05 110

Val Ala Ala Pro Arg Gly Val Tyr Val Ala Pro Gly Gly Ser Leu Met

125

120

115

Leu Val Ser Asp Ser Ala Asp Gly Thr Ile His Arg Tyr Glu Leu Ala Ser Pro Tyr Glu Pro Ala Gly Ala Ala Asn Arg Gly Ser Phe Asp Val 150 155 Ser Asp Met Asp Gly Ser Pro Val Gly Ala Gly Phe Ala Gly Gly Leu 165 170 His Met Tyr Val Ala Gly Asn Asp Thr Gly Arg Val Tyr Gln Tyr Pro 185 Ala Gly Thr His Gln Ile Gln Glu Ala Ala Gly Pro Arg Leu Leu 200 205 Ser Ala Val Leu Asp Lys Asp Gly Thr Leu Arg Ala Ala Phe Asp Gly 215 Thr Val Asp Ala Gly Ser Val Gln Pro Gly Met Ile Thr Ile Arg Asp 235 Gly His Gly Ser Asn Thr Gly Ile Pro Leu Leu Leu Ala Gly Gly Ala 250 Ala Asp Ser Asp Val Met Thr Phe Val Val Pro Glu Lys Asp Arg Ala 265 260 Glu Ala Ala Ala Tyr Gly Asp Gln Ser Leu His Val Pro Ala Ala Ala 280 Leu Ala Gly Thr Gly Gly Gly Pro Phe Val Pro Asp Phe Ser Gly Gly 295 300 Ser Leu Leu Ala Ser Leu Tyr Arg His Glu Arg Pro Phe Gln Gly Glu 310 315 Glu Met Ala Arg Thr Glu Arg Ser Asp Arg Tyr Ala Leu Thr Val Thr 325 330 Ala Gly Gly Ser Gln Met His Val Gly Gly Ala Gly Gly Asn Ile Thr 345 Trp Tyr Asp Leu Gly Thr Pro His Asp Ile Thr Thr Gly Val Arg Ala 360 Gly Ser Asp Ile Leu Pro Ala Tyr Pro Ser Ala Gly Arg Asn Val Val 375 Pro Ser Ile Thr Gly Ile Ala Phe Ser Asp Asp Gly Met Arg Leu Phe 390 395 Ala Ala Asn Arg Gly Asp Arg Ile Pro Met Tyr Gln Leu Asp Ser Pro 405 410 Tyr Asp Ile Gly Ser Ala Ser Leu Glu Gly Thr Leu Phe Thr Gly Phe 425 Gln Ser Gly Ile Ala Phe Ser Asp Asp Gly Thr Arg Met Phe Ala Ala 440 Leu Leu Thr Glu Asn Ala Ile Arg Gln Tyr Asp Leu Glu Gly Pro Tyr 455 460 Asp Ile Arg Gly Ala Gly Asn Ala Gly Gln Tyr Asp Leu Asp Ile Pro 470 475 Leu His Pro Gly Leu Leu Phe Leu Leu Thr Ser Gly Val His Phe Ser 485 490 Pro Asp Gly Thr Arg Met Phe Val Gly Glu Gly Ile Ser Asp Ala Glu 505 Asp Ala Asn Ala Asn Arg Asp Val Asn Val Asn Leu Trp His Arg Phe 520 525 Asp Leu Ser Thr Pro Phe Asp Val Leu Thr Ala Glu Arg Val Asp Thr 535 540 Tyr Glu Tyr Ser Thr Gly Pro Ala Gly Asp Leu Glu Asp Leu Ser Leu Ser Pro Asp Gly Arg Arg Leu Tyr Thr Leu Ser Ser Glu Arg Val Ser 570 565 Ser Ser Glu Tyr Thr Ile Thr Arg Ala Gln Tyr Trp Leu Pro Glu Pro 585

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Tyr	Asp	Val 595		Pro	Pro	Tyr	His 600		Pro	Ser	Phe	Asn 605		Ser	Gln
Gly	Gly 610		Leu	Ala	Asp	Pro 615	Tyr	Gly	Met	Ala	Phe 620		Pro	Asp	Gly
Thr 625	Arg		Leu	Val	Thr 630		His	Gly	Gln	Thr 635			Lys	Leu	Phe 640
		Aan	Dro	D×o		λον	Va l	Glv	ጥኮ~		Va 1	Dhe	ui a	7 00	His
HIS	Deu	- ROII	· FIO	645		vob	Val	Gry	650		101	FIIC	1110	655	nis
Glv	Ara	Phe	Ara			Glv	Pro	λla			Tle	Glu	Δla		Gly
O ₁	1449	1110	660		O ₁	O. y	110	665		JIU		014	670	DCI	GLY
Ile	Ser	Leu			Asp	Glv	Ser			Phe	Leu	Ser		Ara	Gly
		675				1	680	5				685			- 1
Arq	Gly			Ser	Gln	Tvr		Leu	Val	Ala	Pro	_	Asp	Val	Glu
	690					695					700		•		
Phe	Ala	Ser	Asp	Val	Ser	Ala	Asp	Gly	Gln	Leu	Asp	Val	Gly	Ala	Gln
705					710					715					720
Asp	Ala	Leu	Pro	Gly	Gly	Leu	Ala	Phe	Ser	Pro	Gly	Gly	Thr	Arg	Leu
				725					730					735	
Phe	Met	Val	Gly	Gly	Met	Asp	Arg	Ser	Val	His	Met	Tyr	Ser	Leu	Asn
			740					745					750		
Thr	Pro	Phe	Asp	Leu	Gly	Gly	Ala	Glu	His	Ala	Ala	Ser	Phe	Gly	Val
		755					760					765			
Gly	_	Arg	Val	Ser	Asp		Leu	Gly	Ile	Ala		Gly	Asn	Gly	Gly
	770		_			775			- -		780				
	Lys	Met	Leu	Ile		Asp	Thr	Thr	Gly	Phe	Val	His	Gly	Tyr	-
785	~ 3	. 1 -	D	m	790	~ 1 -		~ 1		795			~3		800
Leu	GIY	АТа	Pro	-	Авр	TIE	ser	GIY		Ala	ıyr	ser	GIĀ		Pne
Λcn	ת ות	Clar	Clv	805	Tlo	7 ~~	700	บาไ	810	Val	C1	C1	~1	815	Mak
мър	AIa	GIY	820	ser	TTE	Arg	web	825	Ala	vaı	GIY	GIY	830	ser	Met
Phe	Tle	T.e.u		Glv	Glu	Thr	Δen		Val	Tyr	Gl 11	Hic		Dro	G) v
		835	Oru	OL y	014		840	9	V u _	- 1 -	<u>J</u>	845	my	110	GIY
Ile	Tvr		Val	Val	Ser	Ala	-	Asp	Glv	Pro	Ala		Val	Ser	Ala
	850				-	855		•	- 1		860				
Ala	Ala	Asp	Ala	Arg	Val		Ala	Ala	Glu	Val	Leu	Phe	Asp	Arq	Ala
865		-		-	870	-				875			-	-	880
Val	Asp	Val	Gly	Gly	Ile	Asp	Pro	Gly	Gly	Val	Arg	Ile	Val	Asp	Ala
				885					890					895	
Ala	Gly	Pro	Leu	Pro	Gly	Val	Val	Ile	Ser	Asp	Ala	Val	Ile	Pro	Gly
			900					905					910		
Glu	Asp		Gly	Val	Ala	Arg	Phe	Ser	Leu	Ser	Asp	Ala	Glu	Val	Leu
		915	_				920					925			
Ala		Ser	Gly	Tyr	Ala		Pro	Ser	Leu	Val		Gly	Arg	His	Ala
	930	_,				935		_,	_	_	940				_
	Pro	GIA	Ala	Ala	_	GIA	Thr	Pne	Pro	Ser	GIn	11e	GIA	Asn	
945	~1		**- 7	0 3	950	T 1 -	D	.	D	955	•		51	~1	960
Thr	GIU	Leu	vaı		ser	TIE	Pro	Asn		Thr	ьеи	Asp	Pne	_	Thr
The	T 011	mb	C1	965	77.	Dha	C	37.	970	a 1	mL	17_ 1	**- 7	975	
1111	Leu	IIII	980	Ala	AIA	Pne	ser	985	ASP	Gly	Inr	vaı		Pne	Leu
Cor	7 cn	C1.,		Th.∽	C117	λ~~	V-1		Dwa	Tyr	Com	T 0	990	T1.	D
361	Asp	995	PIO	1111	GIY	ALG	1000		PIO	171	361	1005		116	PIO
Phe	Aen		Ser	Ser	Δla	د ۱ ۵			Glv	Phe	V a 1			Dro	เรา
r 11C	1010		JGI	JEI	A1 a	1015		G L Y	G _L y	FIIC	1020		val	FIO	val
Glv			Asn	Ile	Ala			Ala	Asp	Gly			Met	Len	Val
1025					1030					1035				u	1040
		Glu	Thr	Gly			His	Arq	Tyr	Leu		Arq	Ser	Pro	
	-			1045				-	1050			_		1055	-

Glu	Ile	Gly	Thr 106	_	Phe	Ile	Lys	Ser 106		Leu	Gly	Glu	Phe 107		Glu
Thr	Phe	Ser 107	Ala		Pro	Arg	Val 108	Gln		Leu	Ala	Gly 108	Ile		Phe
C	774 ~		-	W-4	71.	Mat			71 -	C1.,	C1.,		-	C	No.1
ser		-	GTÅ	met	me			AIA	ATA	GIŸ			GIY	ser	Val
	109					109				_	110		_		
	_	Tyr	Ser	Leu	Pro	Ser	Pro	Tyr	Ala			Gly	Ala	Lys	Tyr
110	5				111	0				111	5				1120
Glu	Glu	Thr	Ala	Met	Ile	Gly	Gly	Ser	Pro	Ser	Gly	Leu	Glu	Phe	Ser
				112	5				113	0				113	5
Ser	Asp	Glv	Leu	Ara	Met	Phe	Val	Pro	Asp	Ala	Glv	Ser	Glu	Thr	Ala
		1	114	_					5				1150		
71-	W-1	m			חות	חות	Dro			Ile	C114	C1.,			Dwo
AIA	Vai	_	_	Беп	ALG	AIG		_	OL y		Gry			GIU	110
_	_	115			_		116			~~		116		_	_
Leu			Leu	Pne	Leu	_		GIY	АТА	Glu			Thr	Leu	ser
	1170					117					1180				
Pro	Asp	Gly	Arg	His	Ile	Leu	Val	Pro	Gly	Arg	Pro	Gly	Leu	Ser	Gln
118	5				1190	3				119	5				1200
Tyr	Ser	Leu	Phe	Ser	Thr	Asn	Leu	Glu	Leu	Cys	Ala	Glu	Pro	Arg	Gly
_				120	5				121	0				121	5
Tle	Asp	Glv	Glv	Ser	Cvs	Glu	Asp	Glv	Ile	Tyr	Ala	Phe	Glu	Ser	Pro
		4- /	1220		-7-		_	1225		-1-			1230		
GI v	722	Glar			V=1	Sor				Ser	Tle	Thr) en
Gry	ALG	1235		GIY	Vai	Ser	1240		AI a	DCI	116	1245		ALG	Asp
~1	_			~ 3	~1				Di		0 3				_
GIA			TTE	GIY	GIU			GIY	Pne	Ala			Pro	met	Pro
	1250				_	1255					1260				
Ala	Pro	Val	Met	Glu	Gln	Val	Thr	Leu	Asp	Ser	Arg	Glu	Gly	Thr	Leu
1269					1270						;				12ŖO
Arg	Val	Arg	Leu	qaA	Arg	Thr	Val	qaA	Val	Asp	Thr	Val	Arg	Pro	Tyr
				1285	5				1290)				1295	5
Lys	Met	Trp	Val	Glu	Asp	Ser	Asp	Gly	Ser	Gln	Thr	Thr	Leu	Ala	Asn
_		_	1300)	_			1305	5				1310)	
Ser	Thr	Leu	Leu	Asn	Ala	Glu	Asn	Ser	Asn	Ile	Leu	Leu	Phe	Arq	Leu
		1315					1320					1325			
Δsn	Δen			6 [4	Glv	TAVE			Glv	Tyr	Thr			t/a1	Dhe
····	1330			7114	U	1335				-1-	1340				
7			0	C	D			~1	mb~	Asp			mb	T	Desc
		тър	ser	ser			ьeu	GLY	IIII			ALA	THE	Arg	
1345		_			1350		•	_	_	1355			_		1360
His	Thr		_		_					Ala			_	_	
)					
Ser	Gly	Asp	Val	Pro	Ser	Pro	Ser	Gly	Ile	Glu	Phe	Ser	Asp	Asp	Gly
			1380	1				1385	;				1390)	
Met	Arg	Met	Phe	Val	Thr	Gly	Ile	Gly	Thr	Pro	Gly	Ile	Asn	Ile	Phe
		1395					1400)				1405	i		
Thr	Leu	Ser	Ala	Pro	Phe	αaA	Ile	Thr	Leu	Pro	Lvs	His	Ser	Glv	Ser
	1410					1415					1420			,	
Thr			C1.4	C111	Ton			Car) cn	Leu			. ה	7 02	7.00
		116	GIY	_			vaı	261	Asp			Pne	ALG	ASII	
1425		_	_		1430		_		_	1435		_	_		1440
GIA	Asn	Ser	Leu			Leu	Asp	vaı		Gly	val	Leu	Arg	Val	Tyr
				1445					1450)				1455	i
Ala	Leu	Gly	Asp	qaA	Tyr	Asn	Val	Val	Thr	Gly	Thr	Thr	Gln	Lys	Phe
			1460					1465	;				1470		
Arq	Ile	Thr	Leu	asp	Thr	Thr	Gln	Gly	Ile	Pro	Asn	Ser	Ile	Tyr	Thr
9		1475		-			1480					1485		•	
Ser				Len	Ser				Ala	Tyr				Tle	Asn
	1490	_	- y	u		1495				_	1500	_	·•- 9		-10p
			T C**	C1	E0~			7 c ~	TIA				ጥኮ •-	C1	T1-
	-	val	nen	-			HOII	ush	TTE	Ser		TIIT	TILL	GIU	
1505					1510					1515					1520

Ile	Pro	Tyr	Ser	Leu 152		Arg	Pro	Asp	Pro 153		Thr	Gly	Met	Asp 153	Phe 5
Thr	Pro	Asp	Gly 154	_	Arg	Met	Phe	Leu 154		Thr	Glu	Asn	Gly 155		Asp
Gl n	Tur	T.Ou	Leu	Cor	Gl.	Dro	Dha			Thr	Thr	So~			Leu
GIII	TYL			Ser	GIU	PIO			vai	1111	1111			Pne	Leu
_		1559		_			156					156	-		
Arg	Thr	Ile	Pro	Ile	Asp	Gly	Gly	Ala	Glu	Gly	Ile	Arg	Phe	Val	Asp
	157	0				157	5				158	0			
Asn	Gly	Arq	Gly	Leu	Phe	Val	Pro	Gly	Ala	Asp	Glv	Ile	Ile	Gln	Arg
158	_	_	-		159			•		159					1600
		T 011	Tla	П			~1	- ו ת	Cox		_	T 0	T	a 1	Thr
nıs	GIU	пеп	116			TYL	Gry	AIA			Ser	Leu	Leu		
			_	160			_	_	161					161	
Val	Arg	Asp	Gly	Val	Thr	Asp	Gly	Gly	Pro	Gly	Glu	Asn	Pro	Ala	Ala
			1620)				162	5				1630)	
Gly	Glu	Ile	Arg	Leu	Ala	Gly	Thr	Phe	Asn	Ala	Ser	Asp	Asn	Val	Gln
_		1635				_	1640					164			
Ser	Pro			Tle	Glu	Phe			Asn	Glv	Thr			Dhe	Val
001	1650		O- y	110	O.L.	1659		017	.mp	OT Y	1660	_	Mec	FILE	VAI.
m 1			~1					_	~3	-1 -		-	_		_
	_	Phe	GIY	Ala		-	vaı	Asn	GIU			Leu	ser	Ala	Pro
1669					1670					167					1680
Phe	Asp	Thr	Thr	Leu	Pro	Val	His	Val	Glu	Leu	His	Asp	Ile	Gly	Gly
				1689	5				1690)				1695	5
Gln	Pro	Ala	Val	Asp	Leu	Ala	Phe	Ala	Glu	Asp	Glv	Ara	Thr	Len	Len
			1700					1705			,	5	1710		
T	T	71.			~ 1	m)	*				0	+			_
Leu	Leu	Ala		Asp	GIA	Inr			Pne	Tyr	ser			GIY	qaA
		1715					1720					1725	-		
Ala	${ t Tyr}$	Asp	Ile	Gly	Glu	Ala	Ser	Arg	Thr	Phe	Gln	Val	Pro	Phe	Glu
	1730)				1735	5				1740)			
Asp	Ala	Ala	Glv	Ala	Val	Pro	Glv	Ala	Phe	Tvr	Gln	Pro	Pro	Asp	Gly
1745			4		1750					1759					1760
		Ile	Tla	בות			V C.D.	Gly	720			Cln	T1	37.2.7	
	DCI	110	110	1765		FIIC	ASP	O ₁ y	1770		Asp	GIII	TYT		
~1.		-	~1			_					_	_		1775	
TTE	Pro	Phe			vaı	ser	ıyr			Tnr	Arg	Pro	-		Pro
			1780					1785					1790		
Thr	Gly	Ile	Asp	Phe	Ala	Pro	Asp	Gly	Arg	Trp	Met	Phe	Leu	Ser	Thr
		1795					1800)				1805	5		
Glu	Asn	Gly	Ile	Asp	Gln	Tvr	Leu	Leu	Ser	Ile	Pro	Phe	Asp	Val	Ara
	1810			2-		1815					1820				9
C~~		Thr	T	mb	<i>α</i> 1			Dwo	17-1	7 ~			01	02	**
1825															1840
GIn	Phe	Ala	Asp			Arg	Ala	Leu	Phe	Leu	Ala	Asp	Ser	Glu	Gly
				1845	;				1850)				1855	5
Leu	Ile	Tyr	Asn	Tyr	Asp	Leu	Glu	Asp	Pro	Tyr	Ala	Leu	Asp	Gly	Asn
			1860					1865		-			1870	-	
Thr	Tle	Ser			Phe	Ser				Ser	Val	Met			T.a.ı
		1875			- •••		1880		0-7		•			Val	Deu
~3				_	_				_	_,	_	1885		_	
GIU		Asp	inr	гуs	Arg			ser	Tyr	Glu	Leu	Glu	Phe	Pro	Phe
	1890	1				1895					1900				
Asp	Val	Ser	Ser	Arg	Thr	Arg	Ala	Asp	Thr	Leu	Asp	Ile	Pro	Gln	Ile
1905					1910					1915					1920
Asp	Ser	Pro .	Ara	Hie	Val	Δla	Val	Ser	Met			Δen	Wie	I.a.ı	
						ALG	V 44.				Gry	ASII			-
	m)	•		1925					1930					1935	
тте	Thr	Asn			Phe	GLY				Thr	11e	His	Ser	Tyr	Gly
			1940					1945					1950		
Ile	Ser	Asn .	Asn	Asp	Ile	Ser	Ser	Ala	Ser	Tyr	Ile	Gly	Glu	Glu	Gly
		1955		•			1960					1965			-
Ile		Glu		۷al	Ile				Asn	Phe				Glv	Ara
	1970					1975		-			1980			J	3

		Phe	. Leu	ılle	_		/ Asr	ı Gly	Phe		-	Glr	val	Ile	His
198				~3	199	-			~ ~	199	_	_	_	_	2000
ASP	у туг	met	. ren	200		Arg	ј Туг	asp	201		Ser	Arg	Ser	Let 201	Leu
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	****		202		· IIO	, 61	FIC	202		. FIIC	FIC	, MI	203		Asp
Dhe	Car	. Dha		-	Ton		- Mat		_	. Tla	Cov	. Wha	_	_	Ser
	. DCI	203	_	ALG	пеп	361	204		110	. 116	SEL	204		GTA	ser
Val	Τι			~1		7.~~			Dho		17-1		-	N - 4-	
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206		GIU	Ser	Pne			Pro	vai	Pro			Ala	Asp	Asn	Ser
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TTE	Ser	Asp	rea			GIY	ser	ser	-		Asn	Ala	val		Ser
ui e	C1	~1		208		T	m		209				-1.	209	
nis	GIU	GIY			Inr	Leu	Tyr			val	Leu	Авр			Tyr
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GLY	Ald			Asp	ire	Asp			GIU	Leu	Pro			GIY	Val
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PIO			Pne	GLU	Pne			ASN	GIY	Arg			Tyr	Ile	Gly
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		Arg	Asp	ser			ser	Pro	GTA			Pro	Ala	Gly	Leu
214			01	•	215	-	5		•	215		_			2160
GIII	Arg	Tyr	GIU			iie	Pro	ıyr			Ala	ser	Ala		Phe
71-	Ø1 ==	C	T	216		n1		n\	217		51	_		217	
AId	GIII	ser			TTE	Pne	Asp			Pro	Pne	Asn			Arg
71-	7	~1	2180		7 J	~1	7	2189		D			219		
ATA	ASII			Leu	Ala	GIY			vaı	Pro	Pro		-	Ser	Ile
T 011	Dho	219		~ 1	N		220		m\	**- 1	-1-	220		_	
Leu			Ala	GIY	Asn			Arg	inr	Val			Tyr	Asp	Met
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		HIS	Asp	Leu			Leu	Ser	Pne	Arg		Ser	Phe	Lys	
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ASII	Leu			ser	Tyr	ser			Ата	Pro	Ala	-		GIA	Thr
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urs	GIU	Tyr	Ата			GIU	Pro	Trp		Ile	Arg	Asn	Ala		
71.	~ 3	0	T	2325		.			2330			_	_	2335	
Ald	GIY	ser			TIE	ser	Ala			Gly	Ala	Pro	-	_	Leu
D	-1-		2340			_,		2345				_	2350		
Asp	TTE			Asp	GIY	Thr			His	Thr	Met			Arg	Asp
	_	2355		_		_	2360				_	2365			
νne			GIA	Pro	Ala			Val	Asn	His			Pro	Gly	Gln
	2370					2375					2380				
		Leu	Leu				Pro	Ala	Phe	Ala		Pro	Val	Glu	Glu
2385			_		2390					2395					2400
Glu	Gly	Ala				Leu	Ala			Asp	Asp	Gly	Met	Arg	Met
_,		_ •		2405					2410					2415	
Phe	Val	Ala			Asn	Asn				Gln	Tyr				Ser
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Pro				Glu	Asn				Phe	Ile			-	Leu	Leu
		2435					2440					2445			

Thr	Ala 245	_	Arg	Gly	Pro	Thr 245		/ Leu	ı Val	Phe	Ser 246	_	Glu	Asn	Asp
Phe	Phe	Ser	Thr	Gly	Ala	Arc	Ala	Gln	. Phe	Val	Arq	Gln	Phe	Thr	Thr
246					247		•				5				2480
		Pro	Tvr	Asp			Thr	· Ile	Thr			Asn	Asn	Glv	Leu
	3		-7-	248					249					249	
Tur	Taye	Val	Ser	Val		ตา v	r T.en	Pro			Tle	Δrα	Dhe		
-7-	Dy S	Val	250		nop	Gry		250		ori	110	AL 9	251		FIO
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GIN			Leu	Pro	ser			Asp	Inr	ser			vaı	Arg	Asp
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		Glu	Ile	Val			Leu	Phe	Arg			Gly	Leu	Ser	Val
254					255					255					2560
Gly	Leu	Asn	Glu	Pro	Ser	Pro	Ser	Gly	Phe	Asp	Phe	Ser	Glu	Asp	Gly
				256					257					257	
Met	Glu	Leu	Tyr	Val	Thr	Gly	Ser	Gly	Leu	Val	His	Arg	Tyr	Phe	Leu
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Pro	Ser	Pro	Tyr	Gly	Leu	Glu	Asp	Ala	Ala	Tyr	Gly	Gly	Ser	Phe	His
		259	5				260	0				260	5		
Thr	Phe	Arg	Glu	Ser	Thr	Pro	Leu	Gly	Val	Val	Val	Arg	Gly	Asp	Ala
	261	_				261		_			262	_	-	-	
Met	Phe	Val	Ala	Gly	Asp	Ser	Thr	Asp	Ser	Ile	Leu	Lvs	Tvr	Ser	Leu
2625				•	2630			-		263		•	-		2640
Asn	Ala	Gln	Pro	Val	Glv	Asn	Ile	Thr	His	Ala	Asp	Thr	Ara	Ala	
				264					265		_		J	2655	-
Ile	Ala	Asp	Ara	Ala		Ile	Val	Phe			Met	Ala	Asp		
		<i>F</i>	2660					266					2670		9
Ala	Glu	Tle		Asp	Glv	Δla	Asp			His	Lvs	Ser			Tle
		2679			U- J		268				_,5	2689		Lys	110
Asn	Val			Ile	Ser	Glu			Thr	Va 1	Glv			T.em	There
•р	2690					269					2700	-	111 U	LCu	-y-
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T] _	wia) co	C3	Pro		21-	V-1	C1			27.	T	01	2735	
116	ura	мър			TIE	Ala	vaı	2745		TYL	ALA	Leu	_		Met
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			GIA	Asp	Ser			Ala	ser	Asp			Gly	Val	Val
	2770		_	_	_	2775		_	_	_	2780				
		Ser	Arg	Arg			Val	Asp	Arg			Val	Glu	Glu	_
278 5					2790					2795					2800
Ile	Gly	His	Gly	Val	Ser	Leu	Glu	Ala			Arg	Pro	Ala	Val	Asp
				2805					2810					2815	
Asn	Met	Met	Asp	Thr	Asp	Ser	Ala	Gly	Val	Tyr	Asp	Arg	Ser	Pro	Asp
			2820)				2825	5				2830		
Asp	Gly	Pro	Ala	Val	Ser	Asp	Arg	Ser	Ala	Leu	Gly	Leu	Ala	Arg	Met
		2835					2840)			-	2845	;	_	
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			Asp	Arg	Ser			Asp	Glv	Pro			Ser	Asn	Arc
<i>1</i> 2865			F		2870		F		1	2875			~~*	-	2880
		Leu	Glv	Leu			Met	Ala	Ala			Dro	Δla		
	Q			2885		9			2890		n-9	210		vai 2895	•
Asp 1	Met	Met		Thr		Ser	Ala	G) v			Δεν	Δτα			
F			2900		<u>1</u>			2905		-1-	-10P	_	2910		rah

Asp Gly Pro Ala Ile Ser Asp Arg Ser Ala Leu Gly Leu Ala Arg Met 2920 Ala Ala Asp Arg Pro Ala Val Asp Asp Met Met Asp Thr Gly Ser Glu 2935 2940 Ser Thr Ser Arg Leu Gly Pro Val Asp Arg Pro Glu Ile Val Glu Arg 2955 2950 His Ser Leu Ala Ala Ser Val Tyr Leu Ser Gly Gly Asp Ser Pro Ser 2965 2970 Val Ala Asp Gly His Asp Val Glu Ser Glu Gly Arg Arg Asp Gly Gly 2980 2985 Asp Arg Pro Gly Ile Asp Glu Arg Ile Val Ile Lys Ile Ser Tyr Ser 3000 Arg Gly Ala Ala Asp Ala Pro Arg Val Glu Asp Ala Met Glu Thr Ser 3010 3015 3020 Gly Val Thr Ala Tyr Ser Arg Gly Ala Ala Asp Ala Pro Arg Val Glu 3030 3035 3025 Asp Ala Met Glu Thr Ser Gly Val Thr Val Pro Arg Arg Ser Thr Met 3050 3045 Asp Ala Pro Thr Val Ala Asp Asp His Ser Leu Ala Arg Thr Ala Ser 3060 3065 Ile Ser Glu Gly Asp Ser Pro Thr Phe Ala Glu Ala Arg Arg Ala Asp 3075 3080 3085 Thr Val Gly Asp Ile Asp Glu Val Asp Ala Pro Thr Val Ala Asp Asp 3090 3095 3100 His Ser Leu Ala Arg Ala Ala Ser Ile Ser Glu Gly Asp Ser Pro Thr 3115 3110 Phe Ala Glu Val Arg Arg Ala Asp Thr Val Gly Asp Ile Asp Glu Val 3125 3130 Asp Ala Pro Ala Val Ala Glu Arg Leu Leu Ala Val Leu Gly Leu Gln 3140 3145 3150 Ala Pro Asp Ser Pro Gly Val Trp Asp Thr Val Gly Ile Asp His Ser 3155 3160 Glu Ile Ser Gly Asp Pro Val Pro Glu Pro Arg Val Val Pro Arg Gly 3175 3180 Gly Gly Gly Gly Gly Gly Ser Ser Asn Arg Gly Leu Glu Pro His 3190 . 3195 Gly Gly Gly Tyr Glu Ile Asp Phe Glu Phe Arg Ile Asp Gly Arg Leu 3205 3210 Val Leu Phe Asn Gly Thr Asp Val Leu Ala Glu Ser Gly Lys Asp Leu 3225 3230 Leu Ile Arg Pro Val Phe Arg Pro Glu Gly Ser Phe Asn Ile Phe Asp 3235 3240 3245 Met Glu Val Leu Phe Thr Ala Pro Gly Gly Glu Ile Ser Thr Ala Tyr 3255 Tyr Asn Arg Ala Gly Ile Leu Met Gly Ile Asp Cys Gly Glu Leu Ile 3270 3275 Met Thr Asp Thr Thr Tyr Ser Cys Asp Met Leu Asp Ile Phe Gly Asp 3285 3290 Glu Ile Tyr His Val Glu Arg Leu Asp Ala Phe Asn Gly Met Val Ile 3300 3305 Ser Leu Asp Gly Pro Leu Asp Gly Thr Val Ser Val Ser Leu Arg Asp 3315 3320 3325 Asn His Gly Ile Pro Leu Ala Gln His Arg Leu His Lys Tyr Glu Ile 3335 3340 Leu Ile Leu Asp Ala Ala Glu Asn Arg Pro Leu Ser Val Ser Thr Asp 3350 3355 Pro Lys Pro Val Glu Asp Pro Ser Pro Val Gln His Ile Glu Ser Leu 3365 3370

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Gln Met Asp Pro Glu Pro Val Glu Ser Glu Pro Leu Pro Met Asp Ser 3380 3385 Glu Pro Val Glu Asp Leu Glu Pro Val Gln His Leu Glu Ser Leu Pro 3400 Met Asp Pro Glu Pro Val Glu Asp Leu Glu Pro Val Gln His Leu Glu 3415 3420 Pro Val Gln Gly Ser Pro Pro Val Gln Gly Gly Pro Glu Ser Val Glu 3430 3435 Ser Gly Ile Ala Tyr Thr Leu Trp Gln Phe Leu Ser Gly Leu Leu Asp 3445 3450 Ala Leu Gly Leu Ala Asp Pro Asp Val Gly Ser Val Gln Lys Thr Ser 3465 <210> 5 <211> 819 <212> DNA <213> Cenarchaeum symbiosum <220> <221> CDS <222> (1) . . . (810) <400> 5 atg cat ggg atc gag ggc ggc cgg gga gat atg tcg gag aat ttt gtg 48 Met His Gly Ile Glu Gly Gly Arg Gly Asp Met Ser Glu Asn Phe Val gcg ttt tgc gtg gcg tgc gcc agg gga gtc aca aag gac gag atg aag 96 Ala Phe Cys Val Ala Cys Ala Arg Gly Val Thr Lys Asp Glu Met Lys 20 tat gta gac ggg agg gtc ttc cac aaa gag tgc cat gca agg cac gqc 144 Tyr Val Asp Gly Arg Val Phe His Lys Glu Cys His Ala Arg His Gly 40 ggg cag atc cgc ttc ccc aac cca gag gtc gag cag cgc gtg gcc gag 192 Gly Gln Ile Arg Phe Pro Asn Pro Glu Val Glu Gln Arg Val Ala Glu 50 55 ctg aag gtg gac ctg ata cag atg aga aac cag ctg gcc gag atg aac 240 Leu Lys Val Asp Leu Ile Gln Met Arg Asn Gln Leu Ala Glu Met Asn 65 70 agg gcg tcg ggg gac gga ggg gtg cat tcc agc gcc acc tct gcg gcc 288 Arg Ala Ser Gly Asp Gly Gly Val His Ser Ser Ala Thr Ser Ala Ala 85 gag gee gag cag cac agg gee gag eta aag gta cag etg gtg cag atq 336 Glu Ala Glu Gln His Arg Ala Glu Leu Lys Val Gln Leu Val Gln Met 105 aga aac cag ctg gcc gag atg aac agg aag gcc ccc gga aag ccg gca 384 Arg Asn Gln Leu Ala Glu Met Asn Arg Lys Ala Pro Gly Lys Pro Ala 120 cgg aaa aag gcc gca ggc aag act gca cgg aga aag agc ggc aag aag 432 Arg Lys Lys Ala Ala Gly Lys Thr Ala Arg Arg Lys Ser Gly Lys Lys 130 135 140

	Va]					Gly					Gly				999 Gly 160	480
		_	_							Ala			_		acg Thr	528
_	_	aag Lys	_	_		_	_	_			_	_	_	Ala		576
		agg Arg 195														624
		agg Arg										Lys	_		_	672
		acg Thr														720
		aca Thr														768
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ccts	gctg	at														819
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Met 1	His	Gly	Ile	Glu 5	Gly	Gly	Arg	Gly	Asp 10	Met	Ser	Glu	Asn	Phe 15	Val	
Ala	Phe	Cys	Val 20	Ala	Cys	Ala	Arg	Gly 25	Val	Thr	Lys	Asp	Glu 30	Met	Lys	
Tyr	Val	Asp 35	Gly	Arg	Val		His 40	Lys	Glu	Cys	His	Ala 45		His	Gly	
Gly	Gln 50	Ile	Arg	Phe	Pro			Glu	Val		Gln 60		Val	Ala	Glu	
Leu 65	Lys	Val	Asp	Leu	Ile 70	Gln	Met	Arg	Asn			Ala	Glu	Met	Asn 80	
	Ala	Ser	_	Asp 85		Gly	Val		Ser 90		Ala	Thr	Ser	Ala 95		
Glu	Ala	Glu			Arg	Ala				Val	Gln	Leu	Val 110		Met	
Arg	Asn	Gln 115		Ala	Glu				Lys	Ala	Pro	Gly 125		Pro	Ala	
Arg	Lys	Lys	Ala .	Ala	Gly			Ala	Arg	Arg	Lys		Gly	Lys	Lys	

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Thr Val Arg Arg Lys Thr Gly Lys Arg Thr Ala Gly Lys Lys Ala Gly 145 150 160 Ala Arg Arg Lys Thr Thr Val Lys Arg Thr Ala Arg Arg Lys Thr Thr 165 170 Ala Lys Lys Ala Ala Gly Arg Lys Ala Gly Ala Arg Arg Lys Ala Thr 175 Ala Lys Lys Ala Ala Gly Arg Lys Ala Gly Ala Arg Arg Lys Ala Thr 180 200 205 Ala Arg Arg Thr Val His Lys Lys 11e Gly Val Arg Arg Lys Ser Thr Val Lys Arg Thr Ala Gly Lys Ser Thr Val Arg Arg Lys Ser Thr Val 210 220 Lys Arg Thr Val His Arg Lys Thr Gly Lys Lys Ala Val Val Arg Arg Lys Thr 245 230 235 240 Lys Arg Thr Val Lys Arg Thr Ala Arg Arg Pro Ala Gly Arg Lys Thr 245 250 Pro Gly Arg Ala Ala Arg Arg Ala Gly Ala Lys Arg Arg Arg 255 C210 7 C211 1569 C212 DNA C213 Cenarchaeum symbiosum C220 221 CDS C221 CDS C221 CDS C222 (1) (1569) C400 7 atg cag tcg ctt gga cgg cta gac gag gcg tgc gcg gag ata tcg cgc Met Gln Ser Leu Gly Arg Leu Asp Glu Ala Cys Ala Glu The Ser Arg 1 agc ctg ctt gaa tac gag tcc ccc acc gcc ggt gat gtc cgg acg gag Ser Leu Leu Glu Tyr Glu Ser Pro Thr Ala Gly Asp Val Arg Thr Glu 20 25 30 atc aga agg gca tgc aca aag tac tcg ctc cgg agg atc cas aag aac 11e Arg Arg Ala Cys Thr Lys Tyr Ser Leu Arg Arg The Pro Lys Asn 40 45 cgc gag ata ctg gcc acc gcc agg ggt cag gac ttt gac agg ctg cgc gag ata ctg cgc Arg Glu Ile Leu Ala Thr Ala Arg Gly Gln Asp Phe Asp Arg Leu Arg 50 55 60 ccc ctg ctg ctc aaa aag ccc gta aag acc gca tcc gag gag tgc gcg gag ata ctg cgc Arg Glu Ile Leu Ala Thr Ala Arg Gly Gln Asp Phe Asp Arg Leu Arg 50 55 60 ccc ctg ctg ctc aaa aag ccc gta cag gac tcc cac agg agg tgc acg arg Glu Ile Leu Ala Thr Ala Arg Gly Gln Asp Phe Asp Arg Leu Arg 65 90 95 95 cac gag gtc atg cac atg ccc atg cgc tac gcg tac ccc acc ggc aga tgc aca Ile Ala Val Met Pro Met Pro Tyr Ala Cys Pro His Gly Arg Cys Thr 65 90 95 95 tac tgc ccc ggc ggg gag gcg tcg aac aca ccc acc acc acc acc acc acc gcc acc a		130)				135					140	h			
145	Thr			Arg	Lys	Thr			Arg	Thr	Ala			Lys	Ala	Gly
165	145	•		_	_	150	_	_	_		155		_	-		160
180	Ala	Arg	Arg	Lys			Val	Lys	Arg			Arg	Arg	Lys		
195	Ala	Lys	Lys			Gly	Arg	Lys		_	Ala	Arg	Arg	_		Thr
Ala Arg Arg Thr Ala Gly Lys Ser Thr Val Arg Arg Lys Ser Thr Val 210	Val	Lys			Val	His	Lys	_	Ile	Gly	Val	Arg	-	_	Thr	Thr
Lys Arg Thr Val His Arg Lys Thr Gly Lys Lys Ala Val Val Arg Arg 225 230 230 240 Lys Ser Thr Val Lys Arg Thr Ala Arg Arg Pro Ala Gly Arg Lys Thr 245 250 255 Pro Gly Arg Ala Ala Arg Arg Ala Gly Ala Lys Arg Arg 260 265	Ala		Arg		Ala	Gly			Thr	Val	Arg		Lys		Thr	Val
Lys Ser Thr Val Lys Arg Thr Ala Arg Arg Pro Ala Gly Arg Lys Thr 245 Pro Gly Arg Ala Ala Arg Arg Ala Gly Ala Lys Arg Arg 265		Arg		Val	His	_	Lys	Thr	Gly	Lys	_			Val	Arg	_
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atg cag tcg ctt gga cgg cta gac gag ggg ggg cgg day far ceu Asp Glu Ala Cys Ala Glu Ile Ser Arg Arg Ala Cys Ala Glu Ile Ser Arg Ala Cys Ala Glu Ala Cys Ala Glu Ala Cys Arg Ala Ala Ala Glu Arg Ala Ala <td></td> <td>< 4</td> <td>400></td> <td>7</td> <td></td>		< 4	400>	7												
1	atg				gga	cgg	cta	gac	gag	gcg	tgc	gcg	gag	ata	tcg	cgc
agc ctg ctt gaa tac gag tcc ccc acc gcc ggt gat gtc cgg acg gag Ser Leu Leu Leu Glu Tyr Glu Ser Pro Thr Ala Gly Asp Val Arg Thr Glu 30 atc aga agg gca tgc aca aag tac tcg ctc cgg agg atc cca aag aac lle Arg Arg Ala Cys Thr Lys Tyr Ser Leu Arg Arg lle Pro Lys Asn 40 cgc gag ata ctg gcc acc gcc agg ggt cag gac ttt gac agg ctg cgc Arg Glu Ile Leu Ala Thr Ala Arg Gly Gln Asp Phe Asp Arg Leu Arg 50 ccc ctg ctg ctc aaa aag ccc gta aag acc gca tcc ggg gtg gtg gcc gtg Pro Leu Leu Leu Lys Lys Pro Val Lys Thr Ala Ser Gly Val Ala Val 65 ata gca gtc atg ccc atg ccg tac gcg tgc ccc cac ggc aga tgc aca Ile Ala Val Met Pro Met Pro Tyr Ala Cys Pro His Gly Arg Cys Thr 95 tac tgc ccc ggc ggg ggg gag gcg tcg aac aca aca ccc aac agc tat acc ggc Tyr Cys Pro Gly Gly Glu Ala Ser Asn Thr Pro Asn Ser Tyr Thr Gly 100 ggc gag ccc ata gcg ggc gcg gcc atg aac acc agc ggg tac ccc gga	Met				Gly					Ala					Ser	_
Ser Leu Leu Glu Tyr Glu Ser Pro Thr Ala Gly Asp Val Arg Thr Glu 30 atc aga agg gca tgc aca aag tac tcg ctc cgg agg atc cca aag aac Ile Arg Arg Ala Cys Thr Lys Tyr Ser Leu Arg Arg Ile Pro Lys Asn 35 cgc gag ata ctg gcc acc gcc agg ggt cag gac ttt gac agg ctg cgc Arg Glu Ile Leu Ala Thr Ala Arg Gly Gln Asp Phe Asp Arg Leu Arg 50 ccc ctg ctg ctc aaa aag ccc gta aag acc gca tcc ggg gtg gcc gtg Pro Leu Leu Lys Lys Pro Val Lys Thr Ala Ser Gly Val Ala Val 65 ata gca gtc atg ccc atg ccg tac gcg tgc ccc cac ggc aga tgc aca Ile Ala Val Met Pro Met Pro Tyr Ala Cys Pro His Gly Arg Cys Thr 95 tac tgc ccc ggc ggg gag gcg tcg acc acc acc acc acc acc acc acc ggc Tyr Cys Pro Gly Gly Glu Ala Ser Asn Thr Pro Asn Ser Tyr Thr Gly 110 ggc gag ccc ata gcg ggc ggc ggc acc atg acc acc acc acc acc acc acc acc acc ac	1				5					10					15	
atc aga agg gca tgc aca aag tac tcg ctc cgg agg atc cca aag aac lle Arg Arg Ala Cys Thr Lys Tyr Ser Leu Arg Arg lle Pro Lys Asn 35																
atc aga agg gca tgc aca aag tac tcg ctc cgg agg atc cca aag aac lee agg agg atc cca aag aac lee agg agg ata ctg cgc agg ggt cag ggt cag gac ttt gac agg ctg cgc acg agg ctg cgc acg cfc ccc ctg ctg ctc aaa aag aac acg ccc gta aag acc ccc ctg ctg ctc aaa aag acc ccc gta aag acc ccc ctg ctg ctc aaa aag ccc gta aag acc gca tcc ggg gtg gcc gtg cgc acg ctg ctg ccc ctg ctg Leu Leu Leu Lys Lys Pro Val Lys Thr Ala Ser Gly Val Ala Val acg ccc acg agg ccc acg ccc ccc ctg ctg aaa acc gcc acg ccc ccc ctg ctg aca ccc acc gca tcc acg ccc ccc ccc ccc ccc ccc ccc ccc c	Ser	Leu	Leu		Tyr	Glu	Ser	Pro		Ala	Gly	qaA	Val	_	Thr	Glu
Ile Arg Arg Ala Cys Thr Lys Tyr Ser Leu Arg Arg Ile Pro Lys Asn 35				20					25					30		
cgc gag ata ctg gcc acc gcc agg ggt cag gac ttt gac agg ctg cgc Arg Glu Ile Leu Ala Thr Ala Arg Gly Gln Asp Phe Asp Arg Leu Arg 50 ccc ctg ctg ctc aaa aag ccc gta aag acc gca tcc ggg gtg gcc gtg Pro Leu Leu Leu Lys Lys Pro Val Lys Thr Ala Ser Gly Val Ala Val 65 ata gca gtc atg ccc atg ccg tac gcg tgc ccc cac ggc aga tgc aca Ile Ala Val Met Pro Met Pro Tyr Ala Cys Pro His Gly Arg Cys Thr 85 tac tgc ccc ggc ggg gag gcg tcg aac aca aca ccc aac agc tat acc ggc Tyr Cys Pro Gly Gly Glu Ala Ser Asn Thr Pro Asn Ser Tyr Thr Gly 100 ggc gag ccc ata gcg ggc gcc atg aac acc agc ggg tac gac ccg gaa				-	_		_		_						_	
cgc gag ata ctg gcc acc gcc agg ggt cag gac ttt gac agg ctg cgc Arg Glu Ile Leu Ala Thr Ala Arg Gly Gln Asp Phe Asp Arg Leu Arg 50	TTE	arg		AIA	cys	Tnr	ràa		ser	ьeи	Arg	Arg		Pro	rys	Asn
Arg Glu Ile Leu Ala Thr Ala Arg Gly Gln Asp Phe Asp Arg Leu Arg 50																
ccc ctg ctg ctc aaa aag ccc gta aag acc gca tcc ggg gtg gcc gtg Pro Leu Leu Leu Lys Lys Pro Val Lys Thr Ala Ser Gly Val Ala Val 65				_	_		_			-	_		-		_	_
Pro Leu Leu Leu Lys Lys Pro Val Lys Thr Ala Ser Gly Val Ala Val 65 70 70 75 80 ata gca gtc atg ccc atg ccg tac gcg tgc ccc cac ggc aga tgc aca Ile Ala Val Met Pro Met Pro Tyr Ala Cys Pro His Gly Arg Cys Thr 85 90 95 tac tgc ccc ggc ggg gag gcg tcg aac aca ccc aac agc tat acc ggc Tyr Cys Pro Gly Gly Glu Ala Ser Asn Thr Pro Asn Ser Tyr Thr Gly 100 105 110	3		_ =			-		3	- -1					3		3
ata gca gtc atg ccc atg ccg tac gcg tgc ccc cac ggc aga tgc aca Ile Ala Val Met Pro Met Pro Tyr Ala Cys Pro His Gly Arg Cys Thr 85 90 95 tac tgc ccc ggc ggg gag gcg tcg aac aca ccc aac agc tat acc ggc Tyr Cys Pro Gly Gly Glu Ala Ser Asn Thr Pro Asn Ser Tyr Thr Gly 100 105 110 ggc gag ccc ata gcg gcg ggc gcc atg aac agc ggg tac gac ccg gaa	ccc	ctg	ctg	ctc	aaa	aag	ccc	gta	aag	acc	gca	tcc	999	gtg	gcc	gtg
ata gca gtc atg ccc atg ccg tac gcg tgc ccc cac ggc aga tgc aca Ile Ala Val Met Pro Met Pro Tyr Ala Cys Pro His Gly Arg Cys Thr 85 90 95 tac tgc ccc ggc ggg gag gcg tcg aac aca ccc aac agc tat acc ggc Tyr Cys Pro Gly Gly Glu Ala Ser Asn Thr Pro Asn Ser Tyr Thr Gly 100 105 110 ggc gag ccc ata gcg gcg ggc gcc atg aac agc ggg tac gac ccg gaa		Leu	Leu	Leu	Lys	-	Pro	Val	Lys	Thr		Ser	Gly	Val	Ala	
Ile Ala Val Met Pro Met Pro Tyr Ala Cys Pro His Gly Arg Cys Thr 85 90 95 tac tgc ccc ggc ggg gag gcg tcg aac aca ccc aac agc tat acc ggc Tyr Cys Pro Gly Gly Glu Ala Ser Asn Thr Pro Asn Ser Tyr Thr Gly 100 105 110 110 ggc gag ccc ata gcg gcg ggc gcc atg aac agc ggg tac gac ccg gaa	65					70					75					80
tac tgc ccc ggc ggg gag gcg tcg aac aca ccc aac agc tat acc ggc Tyr Cys Pro Gly Gly Glu Ala Ser Asn Thr Pro Asn Ser Tyr Thr Gly 100 105 110 ggc gag ccc ata gcg gcg ggc gcc atg aac agc ggg tac gac ccg gaa																
tac tgc ccc ggc ggg gag gcg tcg aac aca ccc aac agc tat acc ggc Tyr Cys Pro Gly Gly Glu Ala Ser Asn Thr Pro Asn Ser Tyr Thr Gly 100 105 110 ggc gag ccc ata gcg gcg ggc gcc atg aac agc ggg tac gac ccg gaa	Ile	Ala	Val	Met		Met	Pro	Tyr	Ala		Pro	His	Gly	Arg	-	Thr
Tyr Cys Pro Gly Gly Glu Ala Ser Asn Thr Pro Asn Ser Tyr Thr Gly 100 105 110 ggc gag ccc ata gcg gcg ggc gcc atg aac agc ggg tac gac ccg gaa					0,5					,,					23	
ggc gag ccc ata gcg gcg ggc gcc atg aac agc ggg tac gac ccg gaa													_			
ggc gag ccc ata gcg gcg gcc atg aac agc ggg tac gac ccg gaa	ryr	cys	PLO	-	дТÅ	GIU	ΑΙΑ	ser		rnr	PLO	Asn	ser	-	Thr	GIA

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		115				120					125				
	_	Val	_		 _	_		_	_		His			gat Asp	432
		_		_								_	ttc Phe	atg Met 160	480
	-			_	 		-	_		_		_	gcg Ala 175		528
													aat Asn		576
				_								_	ccg Pro	_	624
													gcc Ala		672
													ttg Leu		720
_						-	-				_		gcc Ala 255	_	768
													gga Gly		816
				-	 	-		-		_	-	_	ctg Leu		864
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	_		Thr	-	 	-							gcc Ala 335		1008
						Arg					Gln		gag Glu		1056

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										7.							
									Pro					Leu		cag Gln	1104
													Cys			ata Ile	1152
2		_										Val	_	_	_	ctc Leu 400	1200
	_		_			-		_	_	_			_	_	tcg Ser 415	ttt Phe	1248
		_										_			cgc Arg	ctg Leu	1296
															gaa Glu		1344
															ctc Leu	ggc Gly	1392
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M	et		00> Ser		Gly	Arg	Leu ·	Asp	Glu	Ala	Cys	Ala	Glu	Ile	Ser	Arg	
	1 er	Leu	Leu	Glu	5 Tyr	Glu	Ser	Pro		10 Ala	Gly	Asp	Val	Arg	15 Thr	Glu	
I	le	Arg		20 Ala	Cys	Thr	Lys	Tyr	25 Ser	Leu	Arg	Arg	Ile	30 Pro	Lys	Asn	
A		Glu 50	35 Ile	Leu	Ala	Thr		40 Arg	Gly	Gln	Asp	Phe 60	45 Asp	Arg	Leu	Arg	

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Pro Leu Leu Lys Lys Pro Val Lys Thr Ala Ser Gly Val Ala Val Ile Ala Val Met Pro Met Pro Tyr Ala Cys Pro His Gly Arg Cys Thr 90 Tyr Cys Pro Gly Glu Ala Ser Asn Thr Pro Asn Ser Tyr Thr Gly 105 Gly Glu Pro Ile Ala Ala Gly Ala Met Asn Ser Gly Tyr Asp Pro Glu 120 Glu Gln Val Arg Ala Gly Leu Ala Arg Leu Arg Ala His Gly His Asp 135 Val Ala Lys Leu Glu Ile Val Ile Val Gly Gly Thr Phe Leu Phe Met 150 Pro Gln Glu Tyr Gln Glu Trp Phe Val Lys Ser Cys Tyr Asp Ala Leu 165 170 Asn Gly Ser Ala Ser Ala Gly Met Glu Glu Ala Lys His Arg Asn Glu 185 Thr Ala Val His Arg Asn Val Gly Leu Thr Ile Glu Thr Lys Pro Asp 200 Tyr Cys Arg Thr Glu His Val Asp Ala Met Leu Gly Phe Gly Ala Thr 215 220 Arg Val Glu Ile Gly Val Gln Ser Leu Arg Glu Glu Val Tyr Leu Arg 230 235 Val Asn Arg Gly His Gly Tyr Gln Asp Val Thr Glu Ser Phe Ala Ala 245 250 Ala Arg Asp Ala Gly Tyr Lys Val Ala Ala His Met Met Pro Gly Leu 265 260 Pro Gly Ala Thr Pro Glu Gly Asp Ile Glu Asp Leu Arg Met Leu Phe 280 Glu Asp Pro Ala Leu Arg Pro Asp Met Leu Lys Val Tyr Pro Ala Leu 295 300 Val Val Arg Gly Thr Pro Met Tyr Glu Glu Tyr Ser Arg Gly Glu Tyr Ser Pro Tyr Thr Glu Glu Glu Val Ile Arg Val Leu Ser Glu Ala Lys 325 330 Ala Arg Val Pro Arg Trp Ala Arg Ile Met Arg Val Gln Arg Glu Ile 345 His Pro Asp Glu Ile Val Ala Gly Pro Arg Ser Gly Asn Leu Arg Gln 360 Leu Val His Lys Arg Leu Gln Glu Gln Gly Arg Arg Cys Arg Cys Ile 375 Arg Cys Arg Glu Ala Gly Leu Ala Gly Arg Thr Val Pro Gln Lys Leu 390 395 Arg Ile Asp Arg Ala Asp Tyr Ser Ala Ser Gly Gly Arg Glu Ser Phe Ile Ser Leu Val Asp Gly Asp Asp Ala Ile Tyr Gly Phe Val Arg Leu 425 Arg Lys Pro Ser Gly Ala Ala His Arg Pro Glu Val Thr Pro Glu Ser 440 Cys Ile Ile Arg Glu Leu His Val Tyr Gly Arg Ser Leu Gly Leu Gly 455 Glu Arg Gly Gly Ile Gln His Ser Gly Leu Gly Arg Arg Leu Val Ser 470 475 Glu Ala Glu Ser Ala Ala Arg Glu Leu Gly Ala Gly Arg Leu Leu Val 490 Ile Ser Ala Val Gly Thr Arg Gly Tyr Tyr Arg Arg Leu Gly Tyr Ser 500 505 Arg Thr Gly Pro Tyr Met Gly Lys Val Leu 520

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Met 1	GIu	Thr	11e	5 5	Arg	GIĀ	Thr	Trp	10	Asp	rys	ьеu	Ala	15	GIU	
					gag Glu											96
					ggc Gly											144
Gly ggg	gat Asp 50	gca Ala	gtc Val	agg Arg	gcg Ala	tac Tyr 55	ggc Gly	gtg Val	gjà aaa	ctc Leu	gcc Ala 60	gtc Val	ggc Gly	gac Asp	atg Met	192
ggg Gly 65	cac His	agc Ser	ttc Phe	cgg Arg	ctc Leu 70	ata Ile	gcg Ala	tac Tyr	ttt Phe	gac Asp 75	gac Asp	ctc Leu	gac Asp	Gly aaa	ctc Leu 80	240
cgc Arg	aag Lys	gtc Val	ccc Pro	gag Glu 85	ggc Gly	atg Met	cca Pro	tcc Ser	tcg Ser 90	cta Leu	gaa Glu	gag Glu	cac His	ata Ile 95	gcc Ala	288
					ata Ile											336
					ggc Gly											384
					agg Arg											432
					cac His 150											480
gag Glu	aag Lys	ata Ile	gcc Ala	gag Glu 165	atg Met	gtg Val	ggc Gly	cag Gln	gaa Glu 170	aag Lys	ttt Phe	cgc Arg	agc Ser	agc Ser 175	ctg Leu	528
					tgt Cys											576

												tac Tyr 205			ggc Gly	624
												Gly			ggc Gly	672
												tgg Trp				720
												gag Glu				768
_	_		_	_		-						gtc Val		_		816
												gag Glu 285				864
												aac Asn				912
												ata Ile				960
												ctc Leu				1008
												gag Glu				1056
							_	_		_	_	aac Asn 365				1104
												ccg Pro				1152
												ttc Phe				1200
												Gly 999				1248
999	ccc	tcg	ccc	ggg	atc	gag	cgg	ctc	ata	gca	ctg	gcc	gga	aac	tat	1296

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Gly Pro Ser Pro Gly Ile Glu Arg Leu Ile Ala Leu Ala Gly Asn Tyr gca gac gac atg tat tot gcc gag aga aca gag gtg gag ott gac ggg 1344 Ala Asp Asp Met Tyr Ser Ala Glu Arg Thr Glu Val Glu Leu Asp Gly 440 gec aca agg ggg gec etc teg gag etg gea gaa atg etc ggt tee gee 1392 Ala Thr Arg Gly Ala Leu Ser Glu Leu Ala Glu Met Leu Gly Ser Ala 450 455 460 ccg gag ggc gga ctg cag gat gtc ata tac ggc gtg gcc aag tcc cac 1440 Pro Glu Gly Gly Leu Gln Asp Val Ile Tyr Gly Val Ala Lys Ser His 465 470 475 ggg gtg ccc ccg cgc gac ttt ttc aag gcg ctg tac agg ata ata ctg 1488 Gly Val Pro Pro Arg Asp Phe Phe Lys Ala Leu Tyr Arg Ile Ile Leu 485 gat gca tcc age ggg ceg agg ata ggc ccc ttc ata gag gac ata ggc 1536 Asp Ala Ser Ser Gly Pro Arg Ile Gly Pro Phe Ile Glu Asp Ile Gly 500 agg gag aag gtg gca ggt atg ata cgg ggg cgc ctc tga 1575 Arg Glu Lys Val Ala Gly Met Ile Arg Gly Arg Leu * 515 <210> 10 <211> 524 <212> PRT <213> Cenarchaeum symbiosum <400> 10 Met Glu Thr Ile Gly Arg Gly Thr Trp Ile Asp Lys Leu Ala His Glu 5 Leu Val Glu Arg Glu Glu Ala Leu Gly Arg Asp Thr Glu Met Ile Asn 25 Val Glu Ser Gly Leu Gly Ala Ser Gly Ile Pro His Met Gly Ser Leu Gly Asp Ala Val Arg Ala Tyr Gly Val Gly Leu Ala Val Gly Asp Met 55 Gly His Ser Phe Arg Leu Ile Ala Tyr Phe Asp Asp Leu Asp Gly Leu 70 Arg Lys Val Pro Glu Gly Met Pro Ser Ser Leu Glu Glu His Ile Ala 85 90 Arg Pro Val Ser Ala Ile Pro Asp Pro Tyr Gly Cys His Asp Ser Tyr 105 Gly Met His Met Ser Gly Leu Leu Leu Glu Gly Leu Asp Ala Leu Gly 120 Ile Glu Tyr Asp Phe Arg Arg Ala Arg Asp Thr Tyr Arg Asp Gly Leu 135 140 Leu Ala Glu Gln Ile His Arg Ile Leu Ser Asn Ser Ser Val Ile Gly Glu Lys Ile Ala Glu Met Val Gly Gln Glu Lys Phe Arg Ser Ser Leu 165 170 Pro Tyr Phe Ala Val Cys Glu Gln Cys Gly Lys Met Tyr Thr Ala Glu 185

Ser Val Glu Tyr Leu Ala Asp Ser Arg Lys Val Arg Tyr Arg Cys Gly

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200
 Asp Ala Glu Val Gly Gly Arg Lys Ile Ala Gly Cys Gly His Glu Gly
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 Glu Ala Asp Thr Gly Gly Ala Gly Gly Lys Leu Ala Trp Lys Val Glu
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                    230
Phe Ala Ala Arg Trp Gln Ala Phe Asp Val Arg Phe Glu Ala Tyr Gly
                                    250
Lys Asp Ile Met Asp Ser Val Arg Ile Asn Asp Trp Val Ser Asp Glu
                                265
Ile Leu Ser Ser Pro His Pro His His Thr Arg Tyr Glu Met Phe Leu
                            280
                                                285
Asp Lys Gly Gly Lys Lys Ile Ser Lys Ser Ser Gly Asn Val Val Thr
                        295
                                            300
Pro Gln Lys Trp Leu Arg Tyr Gly Thr Pro Gln Ser Ile Leu Leu Leu
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Met Tyr Lys Arg Ile Thr Gly Ala Arg Glu Leu Gly Leu Glu Asp Val
Pro Ser Leu Met Asp Glu Tyr Gly Asp Leu Gln Arg Glu Tyr Phe Ala
                                345
Gly Gly Arg Gly Gly Lys Ala Arg Glu Ala Lys Asn Arg Gly Leu
                            360
Phe Glu Tyr Thr Asn Leu Leu Glu Ala Gln Glu Gly Pro Arg Pro His
                        375
                                            380
Ala Gly Tyr Arg Leu Leu Val Glu Leu Ser Arg Leu Phe Arg Glu Asn
                390
                                        395
Arg Thr Glu Arg Val Thr Lys Lys Leu Val Glu Tyr Gly Val Ile Asp
                405
                                   410
Gly Pro Ser Pro Gly Ile Glu Arg Leu Ile Ala Leu Ala Gly Asn Tyr
            420
                                425
Ala Asp Asp Met Tyr Ser Ala Glu Arg Thr Glu Val Glu Leu Asp Gly
Ala Thr Arg Gly Ala Leu Ser Glu Leu Ala Glu Met Leu Gly Ser Ala
                        455
Pro Glu Gly Gly Leu Gln Asp Val Ile Tyr Gly Val Ala Lys Ser His
                    470
                                        475
Gly Val Pro Pro Arg Asp Phe Phe Lys Ala Leu Tyr Arg Ile Ile Leu
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                                   490
Asp Ala Ser Ser Gly Pro Arg Ile Gly Pro Phe Ile Glu Asp Ile Gly
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Arg Glu Lys Val Ala Gly Met Ile Arg Gly Arg Leu
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ctt tca aaa ttg caa cag tat tcg ggg agg gac aca att cta tat qcq
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Leu Ser Lys Leu Gln Gln Tyr Ser Gly Arg Asp Thr Ile Leu Tyr Ala

			20	1				25	i				30)			
			Met	_	_	_	_	His	_			_	Ala		ata Ile	144	i.
		Gly										Arg			aag Lys	192	:
	Lys											ggt			gag Glu 80	240	
			_		_							tat Tyr	_	_		288	
_	-			_		_	-	-		_	_	tcg Ser	_		_	336	
					_	_	_				_	tct Ser 125				384	
												atg Met				432	
												cag Gln		_		480	
												ttg Leu				528	
				_	_			-		_	_	cag Gln			_	576	
						Trp						ttt Phe 205				624	
					Lys							atg Met				672	
												cga Arg				720	
			Gly					Asp				gac Asp	Gln			768	

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cag gat ctg aca ttg tcg gta tct cat gca gcg gat atc ctg tct caa 816 Gln Asp Leu Thr Leu Ser Val Ser His Ala Ala Asp Ile Leu Ser Gln 260 ttt act cca atc aac aaa atc atc gcg aat cac ctc ggt aat tca gtt 864 Phe Thr Pro Ile Asn Lys Ile Ile Ala Asn His Leu Gly Asn Ser Val atc agc aaa cca tca aca tag 885 Ile Ser Lys Pro Ser Thr * 290 <210> 12 <211> 294 <212> PRT <213> Cenarchaeum sybiosum <400> 12 Met Glu Ser Ala Gly Glu Gln Ala Pro Gly Val Val Leu His Asp Tyr 10 Leu Ser Lys Leu Gln Gln Tyr Ser Gly Arg Asp Thr Ile Leu Tyr Ala 25 Thr Asn Trp Met Thr Asp Glu Pro His Thr Pro Asn Glu Ala Leu Ile 40 Thr Asn Gly Asp Leu Tyr Gly Phe Met Arg Met Met Arg Asp Leu Lys 55 60 Thr Lys Lys Leu Asp Leu Ile Leu His Ser Pro Gly Gly Ser Ala Glu 70 Ser Ala Glu Ser Ile Val Thr Tyr Leu His Ala Lys Tyr Asp Asp Ile 90 Arg Val Ile Ile Pro Tyr Ala Ala Met Ser Ala Ala Ser Met Leu Ala 105 Cys Ala Ser Asn Ser Leu Val Met Gly Lys His Ser Ser Ile Gly Pro 120 Ala Asp Pro Gln Phe Ile Phe Pro Thr Lys Ile Gly Met Gln Ile Met 135 Ser Ala Gln Leu Leu Ile Asp Glu Leu Gln Glu Val Gln Val Val Ser 150 155 Glu Lys His Pro Gly Arg Leu Gly Ala Trp Leu Pro Leu Leu Gly Gln 170 Tyr Pro Pro Gly Leu Val Gln Lys Cys Ile Ser Ser Gln Lys Leu Ala 180 185 Glu Val Leu Val Gln Lys Trp Leu Glu Asp His Met Phe Ala Gly Glu 200 Ser Asp Ala Ala Glu Lys Ser Lys Lys Ile Ser Gly Met Leu Ala Ser 215 Pro Gly Lys Tyr Tyr Ser His Gly Arg Tyr Ile Ser Arg Glu Glu Cys 230 235 Arg Gly Ile Gly Leu Lys Ile Thr Asp Leu Glu Ala Asp Gln Glu Phe 250 Gln Asp Leu Thr Leu Ser Val Ser His Ala Ala Asp Ile Leu Ser Gln 265 Phe Thr Pro Ile Asn Lys Ile Ile Ala Asn His Leu Gly Asn Ser Val 280 Ile Ser Lys Pro Ser Thr

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Leu	Arg	Arg 195		Gly	/ Gly	Asp	Lev 200		Cys	· Va]	Ile	e Val 205		ı Pro) Met	
		Gly					Pro					Туг			ggc Gly	672
	Gln					Ser					Phe				gag Glu 240	720
					Arg					Cys		tac Tyr				768
												gtc Val				816
												atg Met 285				864
												att Ile				912
												gcc Ala				960
												aga Arg				1008
												ttc Phe				1056
												cac His 365				1104
Asp												gcc Ala				1152
									Asp			aca Thr				1200
			Leu					Gly				gcc Ala	Ala			1248
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1305

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gga ctg tga Gly Leu *

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<211> 434

<212> PRT

<213> Cenarchaem symbiosum

<400> 14

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Val His Leu Leu His Arg Tyr His Leu Asp Met Ile Thr Arg Asp Gly 390 395 Ile Phe Phe Leu Pro Gly Lys Leu Gly Ala Ile Ser Ala Ala His Ser 405 410 Arg Ala Asp Leu Gly Ala Met Tyr Ser Ala Ser Glu Arg Phe Ala Gly 425 Gly Leu <210> 15 <211> 816 <212> DNA <213> Cenarchaeum symbiosum <220> <221> CDS <222> (1)...(816) <400> 15 atg ata etc tte gge aag age gae eec tee gae etg etc ege eag gee 48 Met Ile Leu Phe Gly Lys Ser Asp Pro Ser Asp Leu Leu Arg Gln Ala gat ctt ttg tgc agt ggg aac aag tac aag gcg gca gtg ggc ctg tac 96 Asp Leu Leu Cys Ser Gly Asn Lys Tyr Lys Ala Ala Val Gly Leu Tyr 20 25 age agg ata etc aag gae gae eeg eag aac agg atg gte etg eag aga Ser Arg Ile Leu Lys Asp Asp Pro Gln Asn Arg Met Val Leu Gln Arg 35 aag ggc ctc gcc ctc aac agg ata aga agg tac tct gat gcc ata acg 192 Lys Gly Leu Ala Leu Asn Arg Ile Arg Arg Tyr Ser Asp Ala Ile Thr 50 55 tgc ttt gat ctg ctc gag ctg gat gat ggc gac gcg cct gca tac 240 Cys Phe Asp Leu Leu Leu Glu Leu Asp Asp Gly Asp Ala Pro Ala Tyr 65 75 aac aac aag gcc ata gcc cag gcc gag ctg ggc gat acg gca tcc gcc 288 Asn Asn Lys Ala Ile Ala Gln Ala Glu Leu Gly Asp Thr Ala Ser Ala 90 ctg gag aac tat ggc agg gcc atc gaa gcc agc ccc agg tac gcg ccg 336 Leu Glu Asn Tyr Gly Arg Ala Ile Glu Ala Ser Pro Arg Tyr Ala Pro 105 gcg tac ttt aac agg gcc gtc ctg ctc gac agg ctc ggc gag cac gaa 384 Ala Tyr Phe Asn Arg Ala Val Leu Leu Asp Arg Leu Gly Glu His Glu 115 120 gac gcg ctg ccg gac ctc gac aag gcg aca agg ctg gac agg gac aag 432 Asp Ala Leu Pro Asp Leu Asp Lys Ala Thr Arg Leu Asp Arg Asp Lys 130 135 140, gcc aac ccg agg ttc tac aag ggg ata gtc ctg gga aag atg ggc cgg 480 Ala Asn Pro Arg Phe Tyr Lys Gly Ile Val Leu Gly Lys Met Gly Arg 145

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				_		-			_				_	_	cac His	528
															ctc Leu	576
			-		-									_	gag Glu	624
	_			-		_			gcc Ala	_		_	_		_	672
	_	_			_				gca Ala		_		_	_		720
-	_	-		_				_	tgg Trp 250	-	_	_		_	_	768
									ttc Phe						taa *	816
	<2 <2	210> 211> 212> 213>	271 PRT	ırcha	eum	symb	oiosu	ım								
	<4	100>	16													
1				5	_		_		Ser 10					15		
Asp	Leu	Leu	20	ser	GIÀ	ASII	гĀг	25	Lys	AIG	Ala	vaı	30	Leu	Tyr	
Ser	Arg	Ile 35	Leu	Lys	Asp	Asp	Pro 40	Gln	Asn	Arg	Met	Val 45	Leu	Gln	Arg	
Lys	Gly 50		Ala	Leu	Asn	Arg 55		Arg	Arg	Tyr	Ser 60		Ala	Ile	Thr	
ayo 8	Phe	qeA	Leu	Leu	Leu 70	Glu	Leu	Asp	Asp	Gly 75	Asp	Ala	Pro	Ala	Tyr 80	
Asn	Asn	Lye	Ala	Ile 85	Ala	Gln	Ala	Glu	Leu 90	Gly	Asp	Thr	Ala	Ser 95	Ala	
Leu	Glu	Asn	Tyr 100		Arg	Ala	Ile	Glu 105	Ala	Ser	Pro	Arg	Tyr 110		Pro	
Ala	Tyr	Phe		Arg	Ala	Val	Leu 120		Asp	Arg	Leu	Gly 125		His	Glu	
Asp	Ala 130		Pro	Asp	Leu	Asp 135		Ala	Thr	Arg	Leu 140		Arg	Asp	Lys	
Ala 145	Asn	Pro	Arg	Phe	Tyr 150	Lys	Gly	Ile	Val	Leu 155	Gly	Lys	Met	Gly	Arg 160	
Hic	Δla	Glu	Δla	T.O.I	Cor	Cve	Dha	Lare	Glu	1/2 l	Cvc	λνα	פות	λen	uio	

His Ala Glu Ala Leu Ser Cys Phe Lys Glu Val Cys Arg Ala Asp His 165 170 175 Gly His Ala Asp Ser Gln Phe His Val Ala Ile Glu Val Ala Glu Leu

185

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Gly Lys His Ala Glu Ala Leu Gly Glu Leu Ala Ala Leu Pro Ala Glu 200 Tyr Arg Glu Asn Ala Asn Val Leu Tyr Ala Arg Ala Arg Ser Leu Ala 215 220 Gly Leu Asp Arg Tyr Asp Glu Ser Ile Ala His Leu Gln Lys Ala Ala 230 235 Arg Lys Asp Ser Lys Thr Ile Lys Lys Trp Ala Arg Ala Glu Lys Ala 250 Phe Asp His Ile Arg Asp Pro Arg Phe Lys Lys Ile Ala Gly 260 265 <210> 17 <211> 696 <212> DNA <213> Cenarchaeum symbiosum <220> <221> CDS <222> (1) ... (696) <400> 17 gtg act gac aag aca agg atc atc gtc ctg cgc aac gcc atg act gaa 48 Met Thr Asp Lys Thr Arg Ile Ile Val Leu Arg Asn Ala Met Thr Glu cag tcc gcc cgg gcc atg atc gag gca aaa aag acg ggg cca ttc agg 96 Gln Ser Ala Arg Ala Met Ile Glu Ala Lys Lys Thr Gly Pro Phe Arg gec atg atg agg geg eec eea aag gag gae gte eat gta eat tee qta 144 Ala Met Met Arg Ala Pro Pro Lys Glu Asp Val His Val His Ser Val agg ctc gtc cac gag gcg ctc atc cgc gtc tcc gcc cgg tac tcg gcc 192 Arg Leu Val His Glu Ala Leu Ile Arg Val Ser Ala Arg Tyr Ser Ala gac ttt ttc aga agg gcc gtg cac ccg atc aag gtg gat cag aac gtg 240 Asp Phe Phe Arg Arg Ala Val His Pro Ile Lys Val Asp Gln Asn Val 65 70 75 atc gag gtg gtg ctg ggc gac ggc gtc ttc ccg ata agg tca aag tcq 288 Ile Glu Val Val Leu Gly Asp Gly Val Phe Pro Ile Arg Ser Lys Ser cgc ata cgc aag acc ctg tcc gcc ggg cgc ggc aag aac agg gtc gat 336 Arg Ile Arg Lys Thr Leu Ser Ala Gly Arg Gly Lys Asn Arg Val Asp 100 105 ctg gaa ctc gag gag cac gta tac gcg gaa tca gag ggc gtg atg tgc 384 Leu Glu Leu Glu Glu His Val Tyr Ala Glu Ser Glu Gly Val Met Cys 115 120 ctt gac cgg cac ggc ggg gag acc ggc ttt ccc tac aag acg ggg acc 432 Leu Asp Arg His Gly Glu Thr Gly Phe Pro Tyr Lys Thr Gly Thr 135

ggc gcg gtc gag ccg tac ccg cgg cgc atg ctt gat tcg tcg gag aat

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Gly 145		Val	Glu	Pro	Туг 150	Pro	Arg	Arg	Met	Leu 155		Ser	Ser	Glu	Asn 160	
			ccg Pro													528
_	_		cgc Arg 180													576
		_	gtc Val	_	_	_	_	_	-							624
			gtg Val													672
	_	_	aaa Lys	_	_	_	_									696
	<: <:	210> 211> 212> 213>	231	ircha	aeum	aymb	oiosı	ım								
		100>														
			_		_					_						
1		_	-	5	Arg				10	_				15		
1		_	Lys Arg 20	5	_				10	_				15		
l Gln	Ser	Ala Met	Arg	5 Ala	Met	Ile	Glu	Ala 25	10 Lys	Lys	Thr	Gly	Pro 30	15 Phe	Arg	
1 Gln Ala	Ser Met Leu	Ala Met 35	Arg 20	5 Ala Ala	Met Pro	Ile Pro Leu	Glu Lys 40	Ala 25 Glu	10 Lys Asp	Lys Val	Thr His Ala	Gly Val 45	Pro 30 His	15 Phe Ser	Arg Val	
1 Gln Ala Arg Asp	Ser Met Leu 50	Ala Met 35 Val	Arg 20 Arg	5 Ala Ala Glu	Met Pro Ala Ala	Ile Pro Leu 55	Glu Lys 40 Ile	Ala 25 Glu Arg	10 Lys Asp Val	Lys Val Ser Lys	Thr His Ala 60	Gly Val 45 Arg	Pro 30 His	15 Phe Ser Ser	Arg Val Ala Val	
I Gln Ala Arg Asp 65	Ser Met Leu 50 Phe	Ala Met 35 Val	Arg 20 Arg His	5 Ala Ala Glu Arg Leu	Met Pro Ala Ala 70	Ile Pro Leu 55 Val	Glu Lys 40 Ile His	Ala 25 Glu Arg Pro	10 Lys Asp Val Ile Phe	Lys Val Ser Lys 75	Thr His Ala 60 Val	Gly Val 45 Arg	Pro 30 His Tyr	15 Phe Ser Ser Asn Lys	Arg Val Ala Val 80	
I Gln Ala Arg Asp 65 Ile	Ser Met Leu 50 Phe Glu	Ala Met 35 Val Phe	Arg 20 Arg His	5 Ala Ala Glu Arg Leu 85	Met Pro Ala Ala 70 Gly	Ile Pro Leu 55 Val	Glu Lys 40 Ile His Gly	Ala 25 Glu Arg Pro Val	10 Lys Asp Val Ile Phe 90	Lys Val Ser Lys 75 Pro	Thr His Ala 60 Val	Gly Val 45 Arg Asp	Pro 30 His Tyr Gln Ser	15 Phe Ser Ser Asn Lys 95	Arg Val Ala Val 80 Ser	
I Gln Ala Arg Asp 65 Ile Arg	Ser Met Leu 50 Phe Glu Ile	Ala Met 35 Val Phe Val	Arg 20 Arg His Arg	5 Ala Ala Glu Arg Leu 85 Thr	Met Pro Ala Ala 70 Gly Leu	Ile Pro Leu 55 Val Asp	Glu Lys 40 Ile His Gly Ala	Ala 25 Glu Arg Pro Val Gly 105	10 Lys Asp Val Ile Phe 90 Arg	Lys Val Ser Lys 75 Pro	Thr His Ala 60 Val Ile Lys	Gly Val 45 Arg Asp Arg	Pro 30 His Tyr Gln Ser Arg	15 Phe Ser Ser Asn Lys 95 Val	Arg Val Ala Val 80 Ser Asp	
I Gln Ala Arg Asp 65 Ile Arg Leu	Ser Met Leu 50 Phe Glu Ile Glu	Ala Met 35 Val Phe Val Arg Leu 115	Arg 20 Arg His Arg Val Lys 100 Glu	5 Ala Ala Glu Arg Leu 85 Thr	Met Pro Ala Ala 70 Gly Leu His	Pro Leu 55 Val Asp Ser Val	Glu Lys 40 Ile His Gly Ala Tyr 120	Ala 25 Glu Arg Pro Val Gly 105 Ala	10 Lys Asp Val Ile Phe 90 Arg	Lys Val Ser Lys 75 Pro Gly Ser	Thr His Ala 60 Val Ile Lys Glu	Gly Val 45 Arg Asp Arg Arg Gly 125	Pro 30 His Tyr Gln Ser Arg 110 Val	15 Phe Ser Ser Asn Lys 95 Val	Arg Val Ala Val 80 Ser Asp Cys	
I Gln Ala Arg Asp 65 Ile Arg Leu	Ser Met Leu 50 Phe Glu Ile Glu Asp 130	Ala Met 35 Val Phe Val Arg Leu 115 Arg	Arg 20 Arg His Arg Val Lys 100 Glu	5 Ala Ala Glu Arg Leu 85 Thr Glu Gly	Met Pro Ala Ala 70 Gly Leu His	Ile Pro Leu 55 Val Asp Ser Val Glu 135	Glu Lys 40 Ile His Gly Ala Tyr 120 Thr	Ala 25 Glu Arg Pro Val Gly 105 Ala	10 Lys Asp Val Ile Phe 90 Arg Glu Phe	Lys Val Ser Lys 75 Pro Gly Ser	Thr His Ala 60 Val Ile Lys Glu Tyr 140	Gly Val 45 Arg Asp Arg Gly 125 Lys	Pro 30 His Tyr Gln Ser Arg 110 Val	15 Phe Ser Ser Asn Lys 95 Val Met	Arg Val Ala Val 80 Ser Asp Cys	
I Gln Ala Arg Asp 65 Ile Arg Leu	Ser Met Leu 50 Phe Glu Ile Glu Asp 130	Ala Met 35 Val Phe Val Arg Leu 115 Arg	Arg 20 Arg His Arg Val Lys 100 Glu	5 Ala Ala Glu Arg Leu 85 Thr Glu Gly	Met Pro Ala Ala 70 Gly Leu His	Ile Pro Leu 55 Val Asp Ser Val Glu 135	Glu Lys 40 Ile His Gly Ala Tyr 120 Thr	Ala 25 Glu Arg Pro Val Gly 105 Ala	10 Lys Asp Val Ile Phe 90 Arg Glu Phe	Lys Val Ser Lys 75 Pro Gly Ser	Thr His Ala 60 Val Ile Lys Glu Tyr 140	Gly Val 45 Arg Asp Arg Gly 125 Lys	Pro 30 His Tyr Gln Ser Arg 110 Val	15 Phe Ser Ser Asn Lys 95 Val Met	Arg Val Ala Val 80 Ser Asp Cys	
I Gln Ala Arg Asp 65 Ile Arg Leu Leu Gly 145	Ser Met Leu 50 Phe Glu Ile Glu Asp 130 Ala	Ala Met 35 Val Phe Val Arg Leu 115 Arg Val	Arg 20 Arg His Arg Val Lys 100 Glu	5 Ala Ala Glu Arg Leu 85 Thr Glu Gly Pro Glu	Met Pro Ala Ala 70 Gly Leu His Gly Tyr 150	Ile Pro Leu 55 Val Asp Ser Val Glu 135 Pro	Glu Lys 40 Ile His Gly Ala Tyr 120 Thr	Ala 25 Glu Arg Pro Val Gly 105 Ala Gly Arg	10 Lys Asp Val Ile Phe 90 Arg Glu Phe Met	Lys Val Ser Lys 75 Pro Gly Ser Pro Leu 155	Thr His Ala 60 Val Ile Lys Glu Tyr 140 Asp	Gly Val 45 Arg Asp Arg Arg Lys Ser	Pro 30 His Tyr Gln Ser Arg 110 Val Thr	15 Phe Ser Ser Asn Lys 95 Val Met Gly Glu Leu	Arg Val Ala Val 80 Ser Asp Cys Thr Asn 160	
I Gln Ala Arg Asp 65 Ile Arg Leu Gly 145 Val	Ser Met Leu 50 Phe Glu Ile Glu Asp 130 Ala Arg	Ala Met 35 Val Phe Val Arg Leu 115 Arg Val Arg	Arg 20 Arg His Arg Val Lys 100 Glu His Glu Pro Arg	5 Ala Ala Glu Arg Leu 85 Thr Glu Gly Pro Glu 165	Met Pro Ala Ala 70 Gly Leu His Gly Tyr 150 Ile	Ile Pro Leu 55 Val Asp Ser Val Glu 135 Pro Asp	Glu Lys 40 Ile His Gly Ala Tyr 120 Thr Arg	Ala 25 Glu Arg Pro Val Gly 105 Ala Gly Arg Gly Arg	10 Lys Asp Val Ile Phe 90 Arg Glu Phe Met Val 170	Lys Val Ser Lys 75 Pro Gly Ser Pro Leu 155 Ala	Thr His Ala 60 Val Ile Lys Glu Tyr 140 Asp Leu	Gly Val 45 Arg Asp Arg Arg Sly 125 Lys Ser Glu	Pro 30 His Tyr Gln Ser Arg 110 Val Thr Ser Lys	15 Phe Ser Ser Asn Lys 95 Val Met Gly Glu Leu 175	Arg Val Ala Val 80 Ser Asp Cys Thr Asn 160 Arg	
I Gln Ala Arg Asp 65 Ile Arg Leu Gly 145 Val	Ser Met Leu 50 Phe Glu Ile Glu Asp 130 Ala Arg Lys	Ala Met 35 Val Phe Val Arg Leu 115 Arg Val Arg Leu	Arg 20 Arg His Arg Val Lys 100 Glu His Glu Pro	Ala Ala Glu Arg Leu 85 Thr Glu Gly Pro Glu 165 Gly	Met Pro Ala Ala 70 Gly Leu His Gly Tyr 150 Ile Pro	Ile Pro Leu 55 Val Asp Ser Val Glu 135 Pro Asp	Glu Lys 40 Ile His Gly Ala Tyr 120 Thr Arg Thr Pro Glu	Ala 25 Glu Arg Pro Val Gly 105 Ala Gly Arg Gly Arg	10 Lys Asp Val Ile Phe 90 Arg Glu Phe Met Val 170 Gly	Lys Val Ser Lys 75 Pro Gly Ser Pro Leu 155 Ala Met	Thr His Ala 60 Val Ile Lys Glu Tyr 140 Asp Leu Arg	Gly Val 45 Arg Asp Arg Asn Gly 125 Lys Ser Glu Asp	Pro 30 His Tyr Gln Ser Arg 110 Val Thr Ser Lys	15 Phe Ser Ser Asn Lys 95 Val Met Gly Glu Leu 175 Arg	Arg Val Ala Val 80 Ser Asp Cys Thr Asn 160 Arg Glu	
I Gln Ala Arg Asp 65 Ile Arg Leu Gly 145 Val Glu	Ser Met Leu 50 Phe Glu Ile Glu Asp 130 Ala Arg Lys Phe Arg	Ala Met 35 Val Phe Val Arg Leu 115 Arg Val Arg Leu Ala 195	Arg 20 Arg His Arg Val Lys 100 Glu His Glu Pro Arg 180	Ala Ala Glu Arg Leu 85 Thr Glu Gly Pro Glu 165 Gly Arg	Met Pro Ala Ala 70 Gly Leu His Gly Tyr 150 Ile Pro Ser	Ile Pro Leu 55 Val Asp Ser Val Glu 135 Pro Asp Pro Val Lys	Glu Lys 40 Ile His Gly Ala Tyr 120 Thr Arg Thr Pro Glu 200	Ala 25 Glu Arg Pro Val Gly 105 Ala Gly Arg Gly Arg Gly Asp 185 Glu	10 Lys Asp Val Ile Phe 90 Arg Glu Phe Met Val 170 Gly Val	Lys Val Ser Lys 75 Pro Gly Ser Pro Leu 155 Ala Met Tyr Arg	Thr His Ala 60 Val Ile Lys Glu Tyr 140 Asp Leu Arg Ala Ile	Gly Val 45 Arg Asp Arg Asn Gly 125 Lys Ser Glu Asp Pro 205	Pro 30 His Tyr Gln Ser Arg 110 Val Thr Ser Lys Leu 190 Val	15 Phe Ser Ser Asn Lys 95 Val Met Gly Glu Leu 175 Arg	Arg Val Ala Val 80 Ser Asp Cys Thr Asn 160 Arg Glu Glu	
I Gln Ala Arg Asp 65 Ile Arg Leu Gly 145 Val Val Glu Ser	Ser Met Leu 50 Phe Glu Ile Glu Asp 130 Ala Arg Lys Phe Arg 210	Ala Met 35 Val Phe Val Arg Leu 115 Arg Val Arg Leu Ala 195 Leu	Arg 20 Arg His Arg Val Lys 100 Glu His Glu Pro Arg 180 Val	Ala Ala Glu Arg Leu 85 Thr Glu Gly Pro Glu 165 Gly Arg Gly	Met Pro Ala Ala 70 Gly Leu His Gly Tyr 150 Ile Pro Ser	Ile Pro Leu 55 Val Asp Ser Val Glu 135 Pro Asp Pro Val Lys 215	Glu Lys 40 Ile His Gly Ala Tyr 120 Thr Arg Thr Pro Glu 200	Ala 25 Glu Arg Pro Val Gly 105 Ala Gly Arg Gly Arg Gly Asp 185 Glu	10 Lys Asp Val Ile Phe 90 Arg Glu Phe Met Val 170 Gly Val	Lys Val Ser Lys 75 Pro Gly Ser Pro Leu 155 Ala Met Tyr Arg	Thr His Ala 60 Val Ile Lys Glu Tyr 140 Asp Leu Arg	Gly Val 45 Arg Asp Arg Asn Gly 125 Lys Ser Glu Asp Pro 205	Pro 30 His Tyr Gln Ser Arg 110 Val Thr Ser Lys Leu 190 Val	15 Phe Ser Ser Asn Lys 95 Val Met Gly Glu Leu 175 Arg	Arg Val Ala Val 80 Ser Asp Cys Thr Asn 160 Arg Glu Glu	

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225 230 <210> 19 <211> 378 <212> DNA <213> Cenarchaeum symbiosum <220> <221> CDS <222> (1)...(378) <400> 19 atg agg tca gaa gag agg ccg ggt cac att gaa aag ttc cta aag agg 48 Met Arg Ser Glu Glu Arg Pro Gly His Ile Glu Lys Phe Leu Lys Arg 10 ged gac aag geg atc gac age geg gtc gag cag ggc gtc aag agg gcc 96 Ala Asp Lys Ala Ile Asp Ser Ala Val Glu Gln Gly Val Lys Arg Ala 25 gac gag ata cta gac gat gca gtc gag ctc ggc aag att acg gtg ggc 144 Asp Glu Ile Leu Asp Asp Ala Val Glu Leu Gly Lys Ile Thr Val Gly 40 gag gcg cag agg agg agc gat gtg ctg ctc aaa cag gcc gag cgg gag 192 Glu Ala Gln Arg Arg Ser Asp Val Leu Leu Lys Gln Ala Glu Arg Glu 50 55 age agg egg etc aag tec aag gge gee aaa aag etc gaa aag gge ata 240 Ser Arg Arg Leu Lys Ser Lys Gly Ala Lys Lys Leu Glu Lys Gly Ile 65 ggc gcc gca aaa aag atg gca gca ggc aag ggc gac gcg ctc gag acg 288 Gly Ala Ala Lys Lys Met Ala Ala Gly Lys Gly Asp Ala Leu Glu Thr 85 ctc gca aag ctc ggc gag ctc aga aag gcg ggg atc ata acg gag aaa 336 Leu Ala Lys Leu Gly Glu Leu Arg Lys Ala Gly Ile Ile Thr Glu Lys 105 100 gag ttt cgc gcc aaa aag aaa aag ctc ctc gca gag atc tga 378 Glu Phe Arg Ala Lys Lys Lys Leu Leu Ala Glu Ile * 120 115 <210> 20 <211> 125 <212> PRT <213> Cenarchaeum symbiosum <400> 20 Met Arg Ser Glu Glu Arg Pro Gly His Ile Glu Lys Phe Leu Lys Arg 10 Ala Asp Lys Ala Ile Asp Ser Ala Val Glu Gln Gly Val Lys Arg Ala 25 Asp Glu Ile Leu Asp Asp Ala Val Glu Leu Gly Lys Ile Thr Val Gly 40 Glu Ala Gln Arg Arg Ser Asp Val Leu Leu Lys Gln Ala Glu Arg Glu

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Ser Arg Arg Leu Lys Ser Lys Gly Ala Lys Lys Leu Glu Lys Gly Ile 70 75 Gly Ala Ala Lys Lys Met Ala Ala Gly Lys Gly Asp Ala Leu Glu Thr Leu Ala Lys Leu Gly Glu Leu Arg Lys Ala Gly Ile Ile Thr Glu Lys 105 Glu Phe Arg Ala Lys Lys Lys Leu Leu Ala Glu Ile 120 <210> 21 <211> 600 <212> DNA <213> Cenarchaeum symbiosum <220> <221> CDS <222> (1) . . . (600) <400> 21 atg tcc cag acg ggg gcc ccg ggc ggg cat gcc tgc acg cca tac acg. 48 Met Ser Gln Thr Gly Ala Pro Gly Gly His Ala Cys Thr Pro Tyr Thr 5 cac gat cac gcc tcg atc gag ctc aag gac gcg tgg gcc tcg tcg agg 96 His Asp His Ala Ser Ile Glu Leu Lys Asp Ala Trp Ala Ser Ser Arg 25 aac gtc egc gag atg tac ttt gtg acc gcc acg ttc tcg tcc gag agc 144 Asn Val Arg Glu Met Tyr Phe Val Thr Ala Thr Phe Ser Ser Glu Ser cag ccg tac ttt gca ccg cag gcc aac cac tac ctg ctg gca agg ttc 192 Gln Pro Tyr Phe Ala Pro Gln Ala Asn His Tyr Leu Leu Ala Arg Phe aag gac gcc ccc aga atg atc aag gcg gtg ggc cgg ggg gag ggc gca 240 Lys Asp Ala Pro Arg Met Ile Lys Ala Val Gly Arg Gly Glu Gly Ala 65 70 tcc tat gtg ttt agc atg gac gag gac ata ttc gag agg gag tcc ccc 288 Ser Tyr Val Phe Ser Met Asp Glu Asp Ile Phe Glu Arg Glu Ser Pro ggg gtg agc tat gta tcg gtg tac tat ctg gag tac ggc gat tcc gag 336 Gly Val Ser Tyr Val Ser Val Tyr Tyr Leu Glu Tyr Gly Asp Ser Glu 100 gag gac ata tgc gag gtg gcg tcc gtg gtg ggg aga aag gag aag ata 384 Glu Asp Ile Cys Glu Val Ala Ser Val Val Gly Arg Lys Glu Lys Ile 115 120 ggc agg gcg gga ata ggg cgc atg gac gtc tgc tcg agg gtg ccg cca 432 Gly Arg Ala Gly Ile Gly Arg Met Asp Val Cys Ser Arg Val Pro Pro 135 aag tit goo tit cog tac age ggg aac ata ata gto oto gag gto too 480 Lys Phe Ala Phe Pro Tyr Ser Gly Asn Ile Ile Val Leu Glu Val Ser

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age gag aag age tac cag age gte aac aag tac tge gag aag acg egg 528 Ser Glu Lys Ser Tyr Gln Ser Val Asn Lys Tyr Cys Glu Lys Thr Arg ege gag gte ate ege aag ggg ata aeg atg ace aac ett gtg age etg 576 Arg Glu Val Ile Arg Lys Gly Ile Thr Met Thr Asn Leu Val Ser Leu 180 tcc ata ctg gag cgg cta aag tag 600 Ser Ile Leu Glu Arg Leu Lys * 195 <210> 22 <211> 199 <212> PRT <213> Cenarchaeum symbiosum <400> 22 Met Ser Gln Thr Gly Ala Pro Gly Gly His Ala Cys Thr Pro Tyr Thr 5 His Asp His Ala Ser Ile Glu Leu Lys Asp Ala Trp Ala Ser Ser Arq Asn Val Arg Glu Met Tyr Phe Val Thr Ala Thr Phe Ser Ser Glu Ser 40 Gln Pro Tyr Phe Ala Pro Gln Ala Asn His Tyr Leu Leu Ala Arg Phe 55 Lys Asp Ala Pro Arg Met Ile Lys Ala Val Gly Arg Gly Glu Gly Ala 70 Ser Tyr Val Phe Ser Met Asp Glu Asp Ile Phe Glu Arg Glu Ser Pro 90 Gly Val Ser Tyr Val Ser Val Tyr Tyr Leu Glu Tyr Gly Asp Ser Glu 105 Glu Asp Ile Cys Glu Val Ala Ser Val Val Gly Arg Lys Glu Lys Ile 120 Gly Arg Ala Gly Ile Gly Arg Met Asp Val Cys Ser Arg Val Pro Pro 135 Lys Phe Ala Phe Pro Tyr Ser Gly Asn Ile Ile Val Leu Glu Val Ser 155 150 Ser Glu Lys Ser Tyr Gln Ser Val Asn Lys Tyr Cys Glu Lys Thr Arg 170 Arg Glu Val Ile Arg Lys Gly Ile Thr Met Thr Asn Leu Val Ser Leu 180 185 Ser Ile Leu Glu Arg Leu Lys 195 <210> 23 <211> 810 <212> DNA <213> Cenarchaeum symbiosum <221> CDS <222> (1)...(810) <400> 23

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1				5					10)				15	5	
				Val					Asp		_	_		Arg	r ctg r Leu	96
			Arg					Ala		_			Ser		ggc Gly	144
ctg Leu	cag Gln 50	Asn	ccg Pro	ccc Pro	gta Val	ata Ile 55	cag Gln	agg Arg	ggc	ggc	agg Arg 60	Gly	ctg Leu	tac Tyr	ctg Leu	192
															gca Ala 80	240
			aag Lys													288
			aag Lys 100													336
			cgg Arg													384
			gcc Ala													432
			tac Tyr													480
cta Leu	gtc Val	ccc Pro	GJÀ aaa	acc Thr 165	ata Ile	tcc Ser	cgg Arg	gac Asp	gag Glu 170	gcg Ala	aca Thr	aag Lys	ctg Leu	tac Tyr 175	cag Gln	528
gcc Ala	gtc Val	ccg Pro	acc Thr 180	gtc Val	tcc Ser	cag Gln	gcg Ala	ctc Leu 185	aag Lys	gtg Val	gcg Ala	ctg Leu	aac Asn 190	ata Ile	tca Ser	576
			cgg Arg			Arg										624
agc Ser	ccc Pro 210	cgc Arg	tcg Ser	ggc Gly	His .	agg Arg 215	atc Ile	ctg Leu	cta Leu	Lys	agg Arg 220	gtg Val	cgc Arg	aag Lys	acg Thr	672
ggc Gly 225	gtc Val	agg Arg	aag Lys	Lys	atc Ile: 230	ccc . Pro	ata (gag Glu	Leu	ggc Gly 235	aag Lys	aac Asn	ggc Gly	Ala	aga Arg 240	720

-70aag ctt gcc cgg gtg gcc gag cgc gag ggc acc gac gag acc cgg ctt Lys Leu Ala Arg Val Ala Glu Arg Glu Gly Thr Asp Glu Thr Arg Leu 245 gcc aac agg ata gtc cgg gag tac ctg agg aag cag cga tga 810 Ala Asn Arg Ile Val Arg Glu Tyr Leu Arg Lys Gln Arg * <210> 24 <211> 269 <212> PRT <213> Cenarchaeum symbiosum

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265

<210> 25 <211> 837 <212> DNA <213> Cenarchaeum symbiosum <220> <221> CDS

<222> (1) ... (837)

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tto		400>			aat	226	+++	ato	. 202	202	att	. 200		~ 2*	aga	4.0
										Thr					Arg	48
				Gln					Val					Ala	ccc	96
			Ala									atc Ile 45			gtc Val	144
												ccc Pro		_		192
	Asn											agg Arg				240
												ggc Gly				288
												gca Ala				336
												acg Thr 125				384
												Gly ggg				432
Ala 145	Ile	Ile	Asn	His	Ser 150	Glu	His	Arg	Val	Pro 155	Ala	gac Asp	Gln	Val	Ala 160	480
Gly	Leu	Val	Pro	Arg 165	Leu	Arg	Gly	Leu	Gly 170	Met	Val	tcg Ser	Val	Val 175	Cys	528
												tat Tyr				576
						Pro						ggc Gly 205				624
										Ala		gag Glu				672
999	gct	ggc	ggc	gta	aag	ctg	ctc	tgc	9 99	gcg	ggc	ata	acc	tcc :	9 99	720

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Gly Ala Gly Gly Val Lys Leu Leu Cys Gly Ala Gly Ile Thr Ser Gly 235 230 gcg gac gtg cgc agg gcc ctc gag ctt ggc tcc gag ggc att ctt gtg 768 Ala Asp Val Arg Arg Ala Leu Glu Leu Gly Ser Glu Gly Ile Leu Val 250 245 gea age ggg gte gta aag teg gea gae eee gea ggg gee ate ggg gag 816 Ala Ser Gly Val Val Lys Ser Ala Asp Pro Ala Gly Ala Ile Gly Glu 265 ctt gcc cgg gcc atg tcc tga 837 Leu Ala Arg Ala Met Ser * 275 <210> 26 <211> 278 <212> PRT <213> Cenarchaeum symbiosum <400> 26 Met Leu Thr Val Phe Gly Lys Phe Ile Thr Thr Ile Arg Leu Asp Arg Ala Val Pro Pro Gln Ala Pro Val His Val Leu Tyr Arg Ala Ala Pro Arg Gly Thr Ala Gly Thr Gly Gly Cys Arg Gly Gly Ile Pro Gly Val Asp Arg Ile Asn Thr Arg Gly Ala Ala Val Arg Ser Pro Val Leu Ile Ile Asn Cys Lys Asn Tyr Glu Glu Ala Ala Gly Gly Arg Ile Arg Gly 70 Leu Ala Asp Ala Ala Ala Gly Ala Ala Ala Arg Tyr Gly Val Arg Ile 90 Ala Ile Ala Pro Pro Gln His Leu Leu Gly Ile Ile Ala Gly Arg Asp 105 Leu Gly Val Leu Ala Gln His Val Asp Asp Lys Gly Thr Gly Ser Thr 120 Thr Gly Tyr Val Val Pro Glu Leu Leu Lys Gln Ser Gly Val Ser Gly 135 140 Ala Ile Ile Asn His Ser Glu His Arg Val Pro Ala Asp Gln Val Ala 150 155 Gly Leu Val Pro Arg Leu Arg Gly Leu Gly Met Val Ser Val Val Cys 170 Val Arg Asp Pro Ala Glu Ala Ala Asp Leu Ser Arg Tyr Cys Pro Asp 185 Tyr Ile Ala Ile Glu Pro Pro Glu Leu Ile Gly Ser Gly Arg Ser Val 200 Ser Thr Glu Arg Pro Gln Val Ile Gln Glu Ala Ala Glu Ala Ile Arg Gly Ala Gly Gly Val Lys Leu Leu Cys Gly Ala Gly Ile Thr Ser Gly 230 235 Ala Asp Val Arg Arg Ala Leu Glu Leu Gly Ser Glu Gly Ile Leu Val 250 245 Ala Ser Gly Val Val Lys Ser Ala Asp Pro Ala Gly Ala Ile Gly Glu 260 265 Leu Ala Arg Ala Met Ser

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-74-<210> 28 <211> 182 <212> PRT <213> Cenarchaeum symbiosum <400> 28 Met Leu Asp Pro Arg Lys Arg Pro Arg Val Val Asn Val Val Ser Thr 10 Ala Asp Leu Gly Arg Arg Val Gly Ala Lys Lys Met Ala Ala Met Pro Cys Cys Met Tyr Asp Glu Ala Val Tyr Gly Gly Arg Cys Gly Tyr Ile 40 Lys Thr Pro Gly Met Arg Gly Arg Val Thr Val Phe Leu Ser Gly Lys Met Ile Ser Val Gly Ala Ser Ser Val Arg Ala Ser Phe Ala Gln Leu 70 75 His Glu Ala Arg Leu His Leu Phe Arg Asn Gly Ala Ala Ala Gly Gly Cys Thr Arg Pro Val Val Arg Asn Met Val Ala Thr Val Asp Ala Gly 105 Arg Thr Val Pro Ile Asp Arg Ile Ser Ser Arg Ile Pro Gly Ala Val 120 Tyr Asp Pro Gly Ser Phe Pro Gly Met Ile Leu Lys Gly Leu Gly Ser 135 Cys Ser Phe Leu Val Phe Ala Ser Gly Lys Val Val Ile Ala Gly Ala 150 155 Arg Ser Pro Gly Glu Leu Tyr Arg Ser Ser Phe Asp Leu Leu Ala Arg 165 170 Leu Asn Gly Ala Gly Ala 180 <210> 29 <211> 2535 <212> DNA <213> Cenarchaeum symbiosum <220> <221> CDS <222> (1)...(2535) <400> 29 gtg acg gtg caa gat gcc gta gag ata ccc ccg tcg ctg ctg gta tct 48 Met Thr Val Gln Asp Ala Val Glu Ile Pro Pro Ser Leu Leu Val Ser 1 5 gca aca tac gac agc cag gca ggg gcg gtc gtc ctc aag ttt tac gag 96 Ala Thr Tyr Asp Ser Gln Ala Gly Ala Val Val Leu Lys Phe Tyr Glu 20 ecg gaa tea caa aag ate gta cae tgg acg gae aat acg ggg cae aag Pro Glu Ser Gln Lys Ile Val His Trp Thr Asp Asn Thr Gly His Lys. ecc tac tgc tat acg agg cag ecc ecc tec gag ett ggg gag ett gaa 192 Pro Tyr Cys Tyr Thr Arg Gln Pro Pro Ser Glu Leu Gly Glu Leu Glu

ggc agg gag gat gtg cta gga acg gag cag gtc atg cgg cac gac ctg

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Gly 65	_	Glu	Asp	Val	Leu 70	_	Thr	Glu	Gln	Val 75		Arg	His	Asp	Leu 80	
	-	_	_	_			_		_				_	_	ccc	288
	_						_		_	_		_		Ile	atg Met	336
_	_		_		-		_							tac Tyr	-	384
_	_	_	_						_	_				aag Lys	_	432
	_		_	_				_		_	_	_	~	ctc Leu	_	480
				_	_	-	_	_	_		_		_	aga Arg 175		528
		_								_	_			cag Gln		576
					-		-		_				_	tca Ser		624
														acg Thr		672
														ctg Leu		720
														gag Glu 255		768
														tcg Ser		816
						Val								ttt Phe		864
_	_		-				_		-			_		gac Asp		912

_			_		_	_		_		-	_	ctc Leu			gga Gly 320	960
_		_	_	_								tca Ser			_	1008
	_			_	_		_	_				aac Asn	_	_		1056
												gtc Val 365				1104
_							_			_		cac His	_		-	1152
_	_				_							ctc Leu	_	_	-	1200
_				_	_		-		_			gat Asp	_	_		1248
												tac Tyr				1296
_	_	_					_			_		ctg Leu 445				1344
_	_			_		_		-		_	_	aaa Lys	_		_	1392
			_	_	_		_					ttt Phe	_	_	_	1440
	_	-			_	_			_			aag Lys				1488
	_				_		_			_	_	tgc Cys		_		1536
			-					_	_			aac Asn 525			_	1584
aca	tcg	atg	ata	atc	ggc	tcg	ctg	cgg	gac	ctg	cgc	gtc	aac	tat	tac	1632

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Thi	530		: Ile	: Ile	e Gly	535		a Arg	J Asp) Lev	54	_	l Ası	туз	Tyr	
	Ser					Thr					Gl				cag Gln 560	1680
					Gln					Val					tac Tyr	1728
				Ala					Leu					Ala	gca Ala	1776
													Thr		tcg Ser	1824
												gac Asp				1872
												gag Glu				1920
cat His	gca Ala	aag Lys	aag Lys	gag Glu 645	cac His	ggt Gly	gtg Val	gag Glu	ctc Leu 650	gaa Glu	gtg Val	gac Asp	aaa Lys	gag Glu 655	tac Tyr	1968
												ttc Phe				2016
												aaa Lys 685				2064
acg Thr	ccc Pro 690	ccg Pro	ttc Phe	ata Ile	aag Lys	gag Glu 695	ctc Leu	ttc Phe	tac Tyr	tcg Ser	ctg Leu 700	ctc Leu	gac Asp	ata Ile	ctc Leu	2112
tca Ser 705	gga Gly	gtc Val	gag Glu	agc Ser	gag Glu 710	gac Asp	gag Glu	ttc Phe	gag Glu	tca Ser 715	gcc Ala	aag Lys	atg Met	agg Arg	atc Ile 720	2160
tca Ser	aag Lys	gcg Ala	Ile .	gcc Ala 725	gcg Ala	tgc Cys	ggc	Lys	agg Arg 730	ctc Leu	gag Glu	gag Glu	agg Arg	cag Gln 735	atc Ile	2208
ccc Pro	ctc Leu	Val	gac Asp 1	ctg Leu	gcg Ala	ttc Phe	Asn	gtg Val 745	atg Met	ata Ile	agc Ser	aag Lys	gcg Ala 750	ccc Pro	tcc Ser	2256
gaa Glu	Tyr	gtc Val 755	aag a Lys '	acc Thr	gtc (Val	Pro (cag Gln 760	cac His	ata Ile	cgg Arg	gcg Ala	gca Ala 765	agg Arg	ctg Leu	ctg Leu	2304

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		Ala			_		_		_			Ser		_	aag Lys	2352
	Met										Met				ggc Gly 800	2400
		_	_		_					_		_	_		gac Asp	2448
_		acc Thr	_								-				_	2496
	_	cag Gln 835										_				2535
		210> 211>														
		212> 213>		rch:	aeum	ermb	ni 081	. m								
				11 0116	acum	3 y iiu	7105	4111								
Met 1		Val		Asp 5	Ala	Val	Glu	Ile	Pro 10	Pro	Ser	Leu	Leu	Val 15	Ser	
Ala	Thr	Tyr	Asp 20	Ser	Gln	Ala	Gly	Ala 25	Val	Val	Leu	Lys	Phe 30	Tyr	Glu	
		Ser 35	Gln	-			40	Trp		-		45	Gly		•	
Pro	Tyr 50	Сув	Tyr	Thr	Arg	Gln 55	Pro	Pro	Ser	Glu	Leu 60	Gly	Glu	Leu	Glu	
Gly 65	Arg	Glu	Asp	Val	Leu 70	Gly	Thr	Glu	Gln	Val 75	Met	Arg	His	Asp	Leu 80	
	Ala	Asp	Lys	Asp 85		Pro	Val	Thr	Lys 90		Thr	Val	Ala	Asp 95		
Leu	Ala	Ile	Gly 100	Gly	Thr	Asn	Ser	Glu 105	Lys	Ser	Ile	Arg			Met	
qaA	Thr	Trp 115		Ser	Asp	Ile	Lys 120		Tyr	Glu	Asn	Tyr 125	110 Leu	Tyr	Asp	
Lys	Ser 130	Leu	Val	Val	Gly	Arg 135	Tyr	Tyr	Ser	Val	Ser 140	Gly	Gly	Lys	Val	
	Pro	His	Asp	Met		Ile	Ser	Asp	Glu		Lys	Leu	Ala	Leu	•	
145 Ser	Leu	Leu	Trp		150 Lys	Val	Val	Asp		155 Gly	Met	Ala	Asp	_	160 Lys	
Glu	Phe	Arg	Glu 180	165 Phe	Ile	Ala	Gly	Trp 185	170 Ala	Asp	Leu	Leu	Asn 190	175 Gln	Pro	
Ile	Pro	Arg 195		Arg	Arg		Ser 200		Asp	Ile	Glu	Val 205		Ser	Glu	
	Gly 210	Arg	Ile	Pro				Ile	Ser	Asp	Arg 220	-	Val	Thr	Ala	
Val 225	Gly	Phe	Ala	Ala	Thr .	Asp	Gly	Leu	_	Gln 235	Val	Phe	Val	Leu	-	
	Gly	Ala	Glu	Glu		Glu	Asn	Gly			Pro	Gly	Val	Glu	240 Val	

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				245					250					255	
Val	Phe	Tyr	Asp 260	Lys	Glu	Ala	Asp	Met 265		Arg	Asp	Ala	Leu 270	Ser	Val
Ile	Gly	Ser 275	Tyr	Pro	Phe	Val	Leu 280	Thr	Tyr	Asn	Gly	Asp 285	Asp	Phe	Asp
Met	Pro 290	Tyr	Met	Leu	Asn	Arg 295	Ala	Arg	Arg	Leu	Gly 300	Val	Ser	Asp	Ser
Asp 305		Pro	Leu	Tyr	Met 310		Arg	qeA	Ser	Ala 315		Leu	Arg	His	Gly 320
	His	Leu	Asp	Leu 325		Arg	Thr	Phe	Ser 330		Arg	Ser	Phe	Gln 335	
Tyr	Ala	Phe	Ala 340		Lys	Tyr	Thr	Asp 345		Ser	Leu	Asn	Ser 350		Thr
Lys	Ala	Met 355	_	Gly	Glu	Gly	Lys 360		Asp	Tyr	Gly	Val	Lys	Leu	Gly
Asp	Leu 370		Leu	Tyr	Gln	Thr 375		Asn	Tyr	Cys	Tyr 380		Asp	Ala	Arg
Leu 385		Leu	Glu	Leu	Ser 390		Phe	Gly		Glu 395		Leu	Met	Asp	Leu 400
	Val	Val	Thr	Ser 405		Ile	Ala	Arg			Ile	Asp	Asp	Met	
Arg	Met	Gly	Val 420		Gln	Trp	Ile	Arg 425		Leu	Leu	Tyr	Tyr 430		His
Arg	Gln	Arg 435	Asn	Ala	Leu	Ile	Pro 440	Arg	Arg	Asp	Glu	Leu 445	Glu	Gly	Arg
Ser	Arg 450	Glu	Val	Ser	Asn	Asp 455	Ala	Val	Ile	Lys	Asp 460	Lys	Lys	Phe	Arg
Gly 465	Gly	Leu	Val	Val	Glu 470	Pro	Glu	Glu	Gly	Ile 475	His	Phe	Asp	Val	Thr 480
Val	Met	Asp	Phe	Ala 485	Ser	Leu	Tyr	Pro	Ser 490	Ile	Ile	Lys	Val	Arg 495	Asn
Leu	Ser	Tyr	Glu 500	Thr	Val	Arg	Cys	Val 505	His	Ala	Glu	Cys	Lys 510	Lys	Asn
		515					520		_		_	52 5	Asn		
	530					535					540		Asn		
545					550					555			Arg		560
				565					570				Ala	575	- •
-			580					585					Pro 590		
		595					600					605	Thr		
	610				_	615					620		Thr		
625			-	_	630					635			Ile		640
His	Ala	Lys	Lys	Glu 645	His	Gly	Val	Glu	Leu 650	Glu	Val	Asp	Lys	Glu 655	Tyr
Arg	Tyr	Val	Val 660	Leu	Ser	Asn	Arg	Lys 665	Lys	Asn	Tyr	Phe	Gly 670	Val	Thr
		675	-		-		680					685	Lys		
Thr	Pro 690	Pro	Phe	Ile	Lys	Glu 695	Leu	Phe	Tyr	Ser	Leu 700	Leu	Asp	Ile	Leu
Ser	Gly	Val	Glu	Ser	Glu	Asp	Glu	Phe	Glu	Ser	Ala	Lys	Met	Arg	Ile

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710 715 Ser Lys Ala Ile Ala Ala Cys Gly Lys Arg Leu Glu Glu Arg Gln Ile Pro Leu Val Asp Leu Ala Phe Asn Val Met Ile Ser Lys Ala Pro Ser 745 Glu Tyr Val Lys Thr Val Pro Gln His Ile Arg Ala Ala Arg Leu Leu 760 Glu Asn Ala Arg Glu Val Lys Lys Gly Asp Ile Ile Ser Tyr Val Lys Val Met Asn Lys Thr Gly Val Lys Pro Val Glu Met Ala Arg Ala Gly 790 795 Glu Val Asp Thr Ser Lys Tyr Leu Glu Phe Met Glu Ser Thr Leu Asp 810 Gln Leu Thr Ser Ser Met Gly Leu Asp Phe Asp Glu Ile Leu Gly Lys 825 Pro Lys Gln Thr Gly Met Glu Gln Phe Phe Lys 840 <210> 31 <211> 555 <212> DNA <213> Cenarchaeum symbiosum <220> <221> CDS <222> (1)...(555) <400> 31 atg ccg ggc ggg ggc agg ctg ccc gtg agc ggc ttt gag cgc cct acc 48 Met Pro Gly Gly Arg Leu Pro Val Ser Gly Phe Glu Arg Pro Thr 1 tgg gat gaa tat ttc atg ctg cag gcg gag ctt gca aag ctc cga tcc 96 Trp Asp Glu Tyr Phe Met Leu Gln Ala Glu Leu Ala Lys Leu Arg Ser 20 aac tgt ata gtc cgc aag gtg ggg gcc gta ata gtg agg gac cac cgg 144 Asn Cys Ile Val Arg Lys Val Gly Ala Val Ile Val Arg Asp His Arg 40 cag ctc gcc aca ggg tat aac ggg acg cct cct ggc gtc aag aac tgc 192 Gln Leu Ala Thr Gly Tyr Asn Gly Thr Pro Pro Gly Val Lys Asn Cys tac gag ggc ggc tgc gag agg tgt gcc gag cgc atc gag ggc agg atc 240 Tyr Glu Gly Gly Cys Glu Arg Cys Ala Glu Arg Ile Glu Gly Arg Ile 65 70 aag tea gge gag gee etg gae egg tge etg tge aac eat gea gag gee 288 Lys Ser Gly Glu Ala Leu Asp Arg Cys Leu Cys Asn His Ala Glu Ala aac gct ata atg cac tgt gcg ata ctc ggg ata ggc gcg ggg ggc ggg 336 Asn Ala Ile Met His Cys Ala Ile Leu Gly Ile Gly Ala Gly Gly 100 ggg gcc acc atg tac acc acg ttc tcg ccg tgt ctg gag tgt acc aag 384 Gly Ala Thr Met Tyr Thr Thr Phe Ser Pro Cys Leu Glu Cys Thr Lys

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<221> CDS

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WO 00/18909 PCT/US99/22752

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	agg Arg															96
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	cag Gln 50	_		_												192
	gcc Ala															240
	gcc Ala															288
	ccc Pro															336
	gag Glu															384
	ttc Phe 130															432
	gcc Ala			Ser					Val		Asp			Arg		480
	ggc	_			_			_				_	-	_		528
	atg Met			_												576
	ccg Pro															624
-	gtg Val 210	_					_	_			_				_	672
ctg	gcc	ctc	gac	gag	agg	tat	tcc	tcc	ctc	aag	agg	tgc	999	tac	gat	720

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Leu 225	Leu	Asp	Glu	Arg 230	_	Ser	Ser	Leu	Lys 235	_	Cys	Gly	туг	Asp 240	
					ctc Leu								_	gtg Val	768
					cgc Arg		_	_	_	_					816
_	_				aac Asn							_	-		864
					agg Arg 295										912
					gac Asp									_	960
					gca Ala						_			_	1008
					gjå aaa	_					_			_	1056
	-	-		_	gac Asp					_				_	1104
					ctg Leu 375			_			_	_			1152
					gag Glu										1200
					acg Thr										1248
	Val		_		ata Ile							_	_		1296
					gly aaa										1344
					aag Lys 455										1392

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att ggt cgg cgc aag atg agc gcc gcc aag ggc atg ggt gag agg atg 1440 Ile Gly Arg Arg Lys Met Ser Ala Ala Lys Gly Met Gly Glu Arg Met 475 470 aac egg teg etg geg gea gge ggg get get gee aag gee get eea aag 1488 Asn Arg Ser Leu Ala Ala Gly Gly Ala Ala Ala Lys Ala Ala Pro Lys 490 1509 gga ctc gag ggg tac ttt tag Gly Leu Glu Gly Tyr Phe * 500 <210> 34 <211> 502 <212> PRT <213> Cenarchaeum symbiosum Met Glu Thr Gly His Ile Thr Gly Arg Tyr Ile Glu Pro Gly Ala Val 10 Glu Arg Arg Asp Tyr Gln Val Gly Leu Ala Glu Gln Ala Ile Arg Glu 25 Asn Cys Ile Val Val Leu Pro Thr Gly Leu Gly Lys Thr Ala Val Ala 45 40 Leu Gln Val Ile Ala His Tyr Leu Asp Glu Gly Arg Gly Ala Leu Phe 55 Leu Ala Pro Thr Arg Val Leu Val Asn Gln His Arg Gln Phe Leu Gly 70 75 Arg Ala Leu Thr Ile Ser Asp Ile Thr Leu Val Thr Gly Glu Asp Thr 90 Ile Pro Arg Arg Lys Lys Ala Trp Gly Gly Ser Val Ile Cys Ala Thr 105 100 Pro Glu Ile Ala Arg Asn Asp Ile Glu Arg Gly Leu Val Pro Leu Glu 120 125 Gln Phe Gly Leu Val Ile Phe Asp Glu Ala His Arg Ala Val Gly Asp 135 Tyr Ala Tyr Ser Ser Ile Ala Arg Ala Val Gly Asp Asn Ser Arg Met 150 155 Val Gly Met Thr Ala Thr Leu Pro Ser Glu Arg Glu Lys Ala Asp Glu 165 170 Ile Met Gly Thr Leu Leu Ser Arg Ser Ile Ala Gln Arg Thr Glu Asp 185 Asp Pro Asp Val Lys Pro Tyr Val Gln Glu Thr Ala Thr Glu Trp Ile 200 Lys Val Asp Leu Pro Pro Glu Met Lys Glu Ile Gln Arg Leu Leu Lys 215 Leu Ala Leu Asp Glu Arg Tyr Ser Ser Leu Lys Arg Cys Gly Tyr Asp 235 230 Leu Gly Ser Asn Arg Ser Leu Ser Ala Leu Leu Arg Leu Arg Met Val 250 Val Leu Gly Gly Asn Arg Arg Ala Ala Lys Pro Leu Phe Thr Ala Ile 265 270 Arg Ile Thr Tyr Ala Leu Asn Ile Phe Glu Ala His Gly Val Thr Pro 280 285 Phe Leu Lys Phe Cys Glu Arg Thr Ser Lys Lys Gly Val Gly Val 295 300

Ala Glu Leu Phe Glu Gln Asp Arg Asn Phe Thr Gly Ala Ile Ala Arg

315

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310

305

305					310					315					320	
Ala	Lys	Ala	Ala	Gln 325	Ala	Ala	Gly	Met	Glu 330	His	Pro	Lys	Ile	Pro 335	Lys	
Leu	Glu	Asp	Ala 340	Val	Arg	Gly	Ala	Arg 345	Gly	Lys	Ala	Leu	Val 350	Phe	Thr	
Ser	Tyr	Arg 355		Ser	Val	Asp	Leu 360		His	Ser	Arg	Leu 365		Ala	Ala	
Gly	Ile 370		Ser	Gly	Ile	Leu 375		Gly	Lys	Ala	Gly 380		Lys	Gly	Leu	
Lys 385		Arg	Lys	Gln	Val 390	-	Thr	Val	Ala	Lys 395		Arg	Asp	Gly	Gly 400	
	Asp	Val	Leu	Val 405		Thr	Arg	Val	Gly 410		Glu	Gly	Leu	Asp 415		
Ser	Glu	Val	Asn 420	Leu	Val	Ile	Phe	Tyr 425		Asn	Val	Pro	Ser 430		Ile	
Arg	Tyr	Val 435		Arg	Arg	Gly	Arg		Gly	Arg	Lys	Asp 445		Gly	Arg	
Leu	Ile 450		Leu	Met	Ala	Lys 455		Thr	Ile	Asp	Glu 460		Tyr	Tyr	Trp	
11e 465		Arg	Arg	Lys	Met 470	Ser	Ala	Ala	Lys	Gly 475	Met	Gly	Glu	Arg	Met 480	
Asn	Arg	Ser	Leu	Ala 485	Ala	Gly	Gly	Ala	Ala 490	Ala	Lys	Ala	Ala	Pro 495	Lys	
Gly	Leu	Glu	Gly 500	Tyr	Phe	,										
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Met 1 gtg	<2 <2 <4 tca ser	220> 221> 222> 400> tcg Ser	CDS (1). 35 tac Tyr	ttt Phe 5	acc Thr	ata Ile	aag Lys gtc	acc Thr ctg Leu	Ala 10 gca	A sn tgc	Leu	Ala	Leu gag Glu	Pro 15 gtg	Asp atg	
Met 1 gtg	<2 <2 <4 tca ser	220> 221> 222> 400> tcg Ser	CDS (1). 35 tac Tyr	ttt Phe 5	acc Thr	ata Ile	aag Lys gtc	acc Thr	Ala 10 gca	A sn tgc	Leu	Ala	Leu	Pro 15 gtg	Asp atg	
Met 1 gtg Val	<2 <2 <4 tca Ser gtc Val	220> 221> 222> 100> tcg Ser aaa Lys	CDS (1). 35 tac Tyr aag Lys 20	ttt Phe 5 tac Tyr	acc Thr aac Asn	ata Ile cac His	aag Lys gtc Val	acc Thr ctg Leu 25	Ala 10 gca Ala atc	Asn tgc Cys	Leu aag Lys	Ala agc Ser	gag Glu 30	Pro 15 gtg Val	Asp atg Met	
Met 1 gtg Val	<2 <2 <4 tca Ser gtc Val	220> 221> 222> 100> tcg Ser aaa Lys	CDS (1). 35 tac Tyr aag Lys 20	ttt Phe 5 tac Tyr	acc Thr aac Asn	ata Ile cac His	aag Lys gtc Val acg Thr	acc Thr ctg Leu 25	Ala 10 gca Ala atc	Asn tgc Cys	Leu aag Lys	Ala agc Ser tct	gag Glu 30	Pro 15 gtg Val	Asp atg Met	96
Met 1 gtg Val	<2 <2 <4 tca Ser gtc Val	220> 221> 222> 100> tcg Ser aaa Lys	CDS (1). 35 tac Tyr aag Lys 20	ttt Phe 5 tac Tyr	acc Thr aac Asn	ata Ile cac His	aag Lys gtc Val	acc Thr ctg Leu 25	Ala 10 gca Ala atc	Asn tgc Cys	Leu aag Lys	Ala agc Ser	gag Glu 30	Pro 15 gtg Val	Asp atg Met	96
Met 1 gtg Val agg Arg	<2 <2 <4 tca Ser gtc Val gcc Ala	220> 221> 222> 100> tcg Ser aaa Lys gag Glu 35	CDS (1) 35 tac Tyr aag Lys 20 aag Lys	ttt Phe 5 tac Tyr cag Gln	acc Thr aac Asn atc Ile	ata Ile cac His cag Gln	aag Lys gtc Val acg Thr 40 caa	acc Thr ctg Leu 25 tcc Ser	Ala 10 gca Ala atc Ile	tgc Cys tcc Ser	Leu aag Lys tcg Ser	Ala agc ser tct ser 45	gag Glu 30 agc Ser	pro 15 gtg Val ggg Gly	atg Met ctc Leu	96
Met 1 gtg Val agg Arg	<2 <2 <4 tca Ser gtc Val gcc Ala aag Lys	220> 221> 222> 100> tcg Ser aaa Lys gag Glu 35	CDS (1) 35 tac Tyr aag Lys 20 aag Lys	ttt Phe 5 tac Tyr cag	acc Thr aac Asn atc Ile	ata Ile cac His cag Gln aag Lys	aag Lys gtc Val acg Thr 40 caa	acc Thr ctg Leu 25 tcc Ser	Ala 10 gca Ala atc Ile	tgc Cys tcc Ser	Leu aag Lys tcg Ser	Ala agc ser tct ser 45	gag Glu 30 agc Ser	pro 15 gtg Val ggg Gly	atg Met ctc Leu	96 144
Met 1 gtg Val agg Arg	<2 <2 <4 tca Ser gtc Val gcc Ala	220> 221> 222> 100> tcg Ser aaa Lys gag Glu 35	CDS (1) 35 tac Tyr aag Lys 20 aag Lys	ttt Phe 5 tac Tyr cag Gln	acc Thr aac Asn atc Ile	ata Ile cac His cag Gln	aag Lys gtc Val acg Thr 40 caa	acc Thr ctg Leu 25 tcc Ser	Ala 10 gca Ala atc Ile	tgc Cys tcc Ser	Leu aag Lys tcg Ser	Ala agc ser tct ser 45	gag Glu 30 agc Ser	pro 15 gtg Val ggg Gly	atg Met ctc Leu	96 144
Met 1 gtg Val agg Arg gac Asp	<2 <2 <4 tca Ser gtc Val gcc Ala aag Lys 50	220> 221> 222> 100> tcg Ser aaa Lys gag Glu 35 tac Tyr	CDS (1). 35 tac Tyr aag Lys 20 aag Lys tcg Ser	ttt Phe 5 tac Tyr cag Gln gag Glu ata	acc Thr aac Asn atc Ile ctc Leu	ata Ile cac His cag Gln aag Lys 55	aag Lys gtc Val acg Thr 40 caa Gln	acc Thr ctg Leu 25 tcc Ser cag Gln	Ala 10 gca Ala atc Ile ttc Phe	tgc Cys tcc Ser aac Asn	Leu aag Lys tcg Ser tcc Ser 60	Ala agc ser tct ser 45 cgg Arg	gag Glu 30 agc Ser ata Ile	Pro 15 gtg Val ggg Gly acc Thr	atg Met ctc Leu gag Glu	96 144
Met 1 gtg Val agg Arg gac Asp	<2 <2 <4 tca Ser gtc Val gcc Ala aag Lys 50	220> 221> 222> 100> tcg Ser aaa Lys gag Glu 35 tac Tyr	CDS (1). 35 tac Tyr aag Lys 20 aag Lys tcg Ser	ttt Phe 5 tac Tyr cag Gln gag	acc Thr aac Asn atc Ile ctc Leu	ata Ile cac His cag Gln aag Lys 55	aag Lys gtc Val acg Thr 40 caa Gln	acc Thr ctg Leu 25 tcc Ser cag Gln	Ala 10 gca Ala atc Ile ttc Phe	tgc Cys tcc Ser aac Asn	Leu aag Lys tcg Ser tcc Ser 60	Ala agc ser tct ser 45 cgg Arg	gag Glu 30 agc Ser ata Ile	Pro 15 gtg Val ggg Gly acc Thr	atg Met ctc Leu gag Glu aag Lys	96 144 192
Met 1 gtg Val agg Arg gac Asp	<2 <2 <4 tca Ser gtc Val gcc Ala aag Lys 50	220> 221> 222> 100> tcg Ser aaa Lys gag Glu 35 tac Tyr	CDS (1). 35 tac Tyr aag Lys 20 aag Lys tcg Ser	ttt Phe 5 tac Tyr cag Gln gag Glu ata	acc Thr aac Asn atc Ile ctc Leu	ata Ile cac His cag Gln aag Lys 55	aag Lys gtc Val acg Thr 40 caa Gln	acc Thr ctg Leu 25 tcc Ser cag Gln	Ala 10 gca Ala atc Ile ttc Phe	tgc Cys tcc Ser aac Asn	Leu aag Lys tcg Ser tcc Ser 60	Ala agc ser tct ser 45 cgg Arg	gag Glu 30 agc Ser ata Ile	Pro 15 gtg Val ggg Gly acc Thr	atg Met ctc Leu gag Glu	96 144 192
Met 1 gtg Val agg Arg gac Asp ttc Phe 65	<pre> </pre> <pre> </pre> <pre> </pre> <pre> <pre> <pre> </pre> <pre> <pre> <pre> <pre> </pre> <pre> <</pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre>	220> 221> 222> 100> tcg Ser aaa Lys gag Glu 35 tac Tyr	CDS (1) 35 tac Tyr aag Lys 20 aag Lys tcg ser tcg ser	ttt Phe 5 tac Tyr cag Gln gag Glu ata	acc Thr aac Asn atc Ile ctc Leu gaa Glu 70	ata Ile cac His cag Gln aag Lys 55 gag Glu	aag Lys gtc Val acg Thr 40 caa Gln ctg Leu	acc Thr ctg Leu 25 tcc Ser cag Gln gaa Glu	Ala 10 gca Ala atc Ile ttc Phe	tgc Cys tcc Ser aac Asn	aag Lys tcg Ser tcc Ser 60	Ala agc ser tct ser 45 cgg Arg	gag Glu 30 agc Ser ata Ile gtg Val	gtg Val ggg Gly acc Thr	atg Met Ctc Leu gag Glu aag Lys 80	96 144 192
Met 1 gtg Val agg Arg gac Asp ttc Phe 65	<pre> </pre> <pre> </pre> <pre> </pre> <pre> </pre> <pre> <pre> <pre> </pre> <pre> <pre> <pre> <pre> </pre> <pre> <pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre>	220> 221> 222> 100> tcg Ser aaa Lys gag Glu 35 tac Tyr	CDS (1) 35 tac Tyr aag Lys 20 aag Lys tcg ser tcg ser	ttt Phe 5 tac Tyr cag Gln gag Glu ata Ile	acc Thr aac Asn atc Ile ctc Leu gaa Glu 70	ata Ile cac His cag Gln aag Lys 55 gag Glu ctg	aag Lys gtc Val acg Thr 40 caa Gln ctg Leu	acc Thr ctg Leu 25 tcc Ser cag Gln gaa Glu	Ala 10 gca Ala atc Ile ttc Phe aag Lys	tgc Cys tcc Ser aac Asn acc Thr 75	Leu aag Lys tcg Ser tcc Ser 60 ggt Gly	Ala agc ser tct ser 45 cgg Arg gcg Ala	gag Glu 30 agc Ser ata Ile gtg Val	Pro 15 gtg Val ggg Gly acc Thr gtc Val	atg Met Ctc Leu gag Glu aag Lys 80	96 144 192 240

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cac gaa ata gac gca ttc tcc gcc gcg ctc acc atg gcc ggc gtg gcc

144

His	Glu	Ile 35		Ala	Phe	Ser	Ala 40		Leu	Thr	Met	Ala 45		Val	Ala	
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_			_				_			_	Met	_			aca Thr 80	240
		_		_		_					_			_	gcc Ala	288
			_	-	_	_						gcg Ala				336
_		_			_		_	_				ttt Phe 125	-	-	_	384
_					_				_	_	_	ggc Gly			~ ~	432
			_	_	_							ggc Gly	_			480
	_					_		-	-	_	_	gtg Val			_	528
		_		_	_		_					tcg Ser			_	576
			_	_		_						gtt Val 205			_	624
				-	_							ccc Pro	_		_	672
												ctg Leu				720
			-	_		_	_			_	_	att Ile		_		768
												cgg Arg				816

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Gln Tyr Phe Asp Gln Ala Tyr Met Leu Lys Asn Gln Thr Val Asp Gly 270 aga aag ctg tcc ata ctg gat gcg gca gta tcc ctc ggg gtg gtg 484 Arg Lys Leu Ser Ile Leu Asp Ala Ala Val Ser Leu Gly Val Gly Val Gly Val 275 ttc acg agt gtc ccg ttc atg caa ggc aag ctg ctc ggg ctc ggg ctg ffe ffhr Ser Val Pro Phe Met Gln Gly Lys Leu Leu Glu Pro Gly Leu 295 ctg ccg gag ttt ggc ggg ctc tcc ccc gcc ctg cdg ctc gag ctc ggt ttc leu Gln Pro Gly Leu 300 ctg ccg gag ttt ggc ggg ctc tcc ser pro Ala Leu Arg Ser Leu Gln Phe Gly Gly Leu Ser Pro Ala Leu Arg Ser Leu Gln Phe 315 atc agg tct acc aggc gtg gtg ctc gcc gcg ggg cac atc cta leu Arg Ser Leu Gln Phe 325 gct gcg cat aca gac gag aac ctc aag atc atg gcg gtg cac acc tca loos 325 gct gcg cat aca gac gag acc ctc aag atc atg gcg gtg ccc ccc atc Ala Ala His Thr Asp Glu Asn Leu Lys Ile Met Gly Val Pro Pro Ile 355 gct gcg ct gac acc tcc ggg gag ctt gtg gcc acc acc tcg tgg tcg ccc ccc atc Ala Ala His Thr Asp Glu Asn Leu Luy Ile Met Gly Val Pro Pro Ile 350 ccc ct gac acc acc acc acc acc acc acc acc acc					Asn					Phe					Phe		768
Arg Lys Leu Ser Ile Leu Asp Ala Ala Val Ser Leu Gly Val Gly Val Cly 275 ttc acg act gat to ccg ttc atg cas gac asg ctg ctc gag cct ggc ctg 290 ttc acg act gac tt ggc ggg ctc tc ccg cc ccg ccc ctg cag ttc leu Glu Pro Gly Leu 295 ctg ccg gag ttt ggc ggg ctc tc cc ccc gcc ctg cag tcc ctg cag ttt ggc ggg ctc tc sag ccc ggc ctg ccc ctg cag ttt leu Ala Pro Ala Leu Arg Ser Leu Glu Phe 310 atc acg tct aca cca ggc gtg ctt Leu Ala Pro Leu Pro Gly His Asn Ser 325 gct gcg cat aca gac gag acc ctc acg ccc ctg ccg ggg cac acc acc tca loos lle Arg Ser Thr Pro Gly Val Leu Ala Pro Leu Pro Gly His Asn Ser 335 gct gcg cat aca gac gag acc ctc acg acg acc ctc acg ggg gtg ctc leu Lys lle Met Gly Val Pro Pro Ile 350 ccc gct gac aca tag ltc ggg gag ctt geu Val Ala Ser Leu Thr Ser Trp Ser 365 ccc ggt cag aca tag ltc ggg gag ctt leu Val Ala Ser Leu Thr Ser Trp Ser 365 ccc ggt cag aca tag ltc ggg gag ctt leu Val Ala Ser Leu Thr Ser Trp Ser 370 ccc gct cag aca tag ltc ggg gag ctt leu Val Ala Ser Leu Thr Ser Trp Ser 365 ccc ggt cag aca tag ltc ggr cac acc ctc acc tcg tgg tcg llo4 ccc ggt cag aca tag ltc ser lau Val Ala Ser Leu Thr Ser Trp Ser 365 ccc ggt cag cac aca tag llo4 ccc ggt cag aca tag llo5 ccc ggt cag cac acc tag llo4 ccc ggt cag acc acc ltc llo6 ccc ggt cag cac acc ltc llo6 ccc ggt cag acc acc ltc llo6 ccc ggt cag acc acc ltc llo6 ccc ggt cag ltc ggg gag ctt gcc ltc llo6 ccc ggt cag cac acc ltc llo6 ccc ggt cag acc acc ltc llo6 ccc ggt cag ltc ltc ltc llo6 ccc ltc ltc ltc ltc ltc ltc llo6 ccc ltc ltc ltc ltc ltc ltc ltc ltc ltc				Asp					Leu					Val			816
Phe Thr Ser Val Pro Phe Met Gln Gly Lys Leu Leu Glu Pro Gly Leu 295	_	_	Leu					Ala					Gly				864
Leu Pro Glu Pro Glu Pro Glu Str. Str. Str. Str. Str. Str. Str. Str.		Thr					Met					Leu					912
The Arg Ser Thr Pro Gly Val Leu Ala Pro Leu Pro Gly His Ash Ser 335	Leu					Gly					Leu					Phe	960
Ala Ala His Thr Asp Glu Asn Leu Lys Ile Met Gly Val Pro Pro Ile 340					Pro					Pro					Asn		1008
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Pro Gly Gln Lys * 370 <210> 40 <211> 372 <212> PRT <213> Cenarchaeum symbiosum <400> 40 Met Ile Ser Gly His Ala Thr Ala Glu Gly Thr Arg Arg Ile Ala Glu 1	_		qaA	_				Leu					Thr				1104
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1 5 10 15 Met Ser Gly Ala His Ile Asp Asn Tyr Lys Met Val Asp Gly Leu His 20 25 30 Leu Ser Asn Val Gly Met Gly Thr Tyr Leu Gly Asp Ala Asp Asp Ala 35 40 45																	
Met Ser Gly Ala His Ile Asp Asn Tyr Lys Met Val Asp Gly Leu His 20 25 30 Leu Ser Asn Val Gly Met Gly Thr Tyr Leu Gly Asp Ala Asp Asp Ala 35 40 45		Ile	Ser	Gly		Ala	Thr	Ala	Glu	_	Thr	Arg	Arg	Ile		Glu	
Leu Ser Asn Val Gly Met Gly Thr Tyr Leu Gly Asp Ala Asp Asp Ala 35 40 45		Ser	Gly		_	Ile	Asp	Asn	_		Met	Val	Asp	-		His	
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Ser Arg Asp Gln Ile Phe Ile Ser Thr Lys Ala Gly Tyr Val Thr Asn
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Ala Gly Gly Asp Asn His Gly Phe Lys Phe Ile Gln Leu Pro Phe Asn
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Leu Pro Glu Phe Gly Gly Leu Ser Pro Ala Leu Arg Ser Leu Gln Phe
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Ile Arg Ser Thr Pro Gly Val Leu Ala Pro Leu Pro Gly His Asn Ser
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Ala Ala His Thr Asp Glu Asn Leu Lys Ile Met Gly Val Pro Pro Ile
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Asp Ala Arg Glu Val Leu Pro Arg Leu Ala Lys Asn Thr Ala Glu Arg
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					_	_						tgc Cys	_	_	_	240
		_	_		_							gat Asp				288
	_		-	_	_	_	_					cta Leu		_		336
-						_		_				tac Tyr 125	_	_		384
				_								gcg Ala				432
						_	_			_		gac Asp			_	480
		_	_				-	_	-			aac Asn	_			528
				_	_		-			_		gat Asp			_	576
												cct Pro 205				624
												gcc Ala				672
				Tyr					Tyr			ttc Phe				720
_			Lys					His				ccg Pro	Ile		_	768
gca	tgc	aac	ccg	cgg	ggc	aag	aac	ccg	999	aac	gtc	tgg	gag	ata	tcc	816

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Ala	Суз	Asn	Pro 260	Arg	Gly	Lys	Asn	Pro 265	Gly	Asn	Val	Trp	Glu 270	Ile	Ser	
												ttc Phe 285				864
												ggc Gly				912
												gtc Val				960
	_	~ ~						_	_			gcc Ala			-	1008
	~		-			_	_		_	_		cgg Arg				1056
_			_	_		_				_	_	acc Thr 365				1104
tga *										•						1107
	<2 <2	10> 11> 12>	368	rcha	eum	symb	oiosu	ım								

<400> 42

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Ala Asn Asp Arg Leu Gln Phe Ala Pro Gly Lys Arg Asp Pro Glu Ala 180 185 Ile Gly Arg Ile Ala Ala Val Ile His Gly Ser Thr Pro Gly Thr Pro 200 Phe Asp Glu Leu Pro Thr Thr Gly Glu Ile Ser Trp Ala His Gly Tyr 215 Asp Pro Glu Lys Tyr Cys Pro Thr Cys Tyr Arg Lys Phe Arg Arg His 230 235 Ala Thr Arg Lys Arg Ile Gly Gly His Glu His Tyr Pro Ile Phe Ala 250 Ala Cys Asn Pro Arg Gly Lys Asn Pro Gly Asn Val Trp Glu Ile Ser 265 Thr Lys Ala His His Gly Asn Glu His Phe Ala Val Phe Pro Glu Asp 275 280 285 Leu Val Ser Arg Ile Val Lys Phe Ala Thr Lys Glu Gly Asp Tyr Val 295 Leu Asp Pro Phe Ala Gly Arg Gly Thr Thr Gly Ile Val Ser Ala Cys 310 315 Leu Lys Arg Gly Phe Thr Gly Ile Asp Leu Tyr Pro Ala Asn Val Ala Arg Ala Arg Arg Asn Val Gln Asp Ser Ala Asp Ser Arg Leu Ser Lys 340 345 Lys Val Leu Asp Gln Ile Met Pro Glu Arg Gln Leu Thr Gly Tyr Phe 360 <210> 43 <211> 933 <212> DNA <213> Cenarchaeum symbiosum <220> <221> CDS <222> (1)...(933) <400> 43 atg cet agt tae gea gaa ata gea aac gae gta ett ega eta atg gaq 48 Met Pro Ser Tyr Ala Glu Ile Ala Asn Asp Val Leu Arg Leu Met Glu tca gtc ggt gag cag gca cct ggt gta gta ctt cac gac tat ctt tca 96 Ser Val Gly Glu Gln Ala Pro Gly Val Val Leu His Asp Tyr Leu Ser 20 30 aaa ttg caa cag tat tcg ggg agg gat aca ata ctg tat gcg acc aac 144 Lys Leu Gln Gln Tyr Ser Gly Arg Asp Thr Ile Leu Tyr Ala Thr Asn 35 tgg ata acg gac gaa gcg cat acg tct aat gaa gct ctc ata aca aat 192 Trp Ile Thr Asp Glu Ala His Thr Ser Asn Glu Ala Leu Ile Thr Asn 50 ggt gac ctg tat gga ttt atg agg atg atg cgt gat tta aaq act aaq 240 Gly Asp Leu Tyr Gly Phe Met Arg Met Met Arg Asp Leu Lys Thr Lys 70 aaa tta gat tta ata ctc cac agt ccg ggg ggc tcc gtc gag tcc acc 288 Lys Leu Asp Leu Ile Leu His Ser Pro Gly Gly Ser Val Glu Ser Thr

			_				_						_	Arg	atc Ile		336
				_		_	_	_	_		_		-	_	tca Ser		384
															gac Asp		432
						acc Thr				_			_		gca Ala 160		480
						ttt Phe								-			528
						gca Ala				_							576
						tgc Cys		_	_	_	_		_		_		624
	-				_	gct Ala 215	_		_						_		672
	_		_			aaa Lys			-		_						720
			_			agg Arg	_		_	_	_	-	_				768
	-			-		gat Asp	_	-	-	-		-			_		816
_		_		_		cat His		_			_		_				864
						atg Met 295							_	_			912
aca Thr 305	_		aca Thr	Pro		taa *										!	933

WO 00/18909 PCT/US99/22752

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<211> 310 <212> PRT

<213> Cenarchaeum symbiosum

<400> 44

Met Pro Ser Tyr Ala Glu Ile Ala Asn Asp Val Leu Arg Leu Met Glu Ser Val Gly Glu Gln Ala Pro Gly Val Val Leu His Asp Tyr Leu Ser 25 Lys Leu Gln Gln Tyr Ser Gly Arg Asp Thr Ile Leu Tyr Ala Thr Asn 40 Trp Ile Thr Asp Glu Ala His Thr Ser Asn Glu Ala Leu Ile Thr Asn Gly Asp Leu Tyr Gly Phe Met Arg Met Met Arg Asp Leu Lys Thr Lys 70 75 Lys Leu Asp Leu Ile Leu His Ser Pro Gly Gly Ser Val Glu Ser Thr 90 Glu Ala Ile Val Ser Tyr Ile Arg Ala Lys Phe Lys Asn Val Arg Ile 105 100 Ile Ile Pro Tyr Ala Ala Met Ser Ala Ala Ala Met Leu Ala Cys Ser 120 125 Ser Asn Cys Leu Val Met Gly Lys His Ser Ser Ile Gly Pro Thr Asp 135 140 Pro Gln Phe Ile Ile Pro Thr Arg Thr Gly Met His Ile Met Ser Ala 150 155 Gln Phe Leu Ile Ser Glu Phe Gln Glu Ala Gln Ser Val Ser Glu Lys 170 His Pro Gly Arg Leu Gly Ala Trp Leu Pro Leu Leu Gly Gln Tyr Pro Pro Gly Leu Ile Gln Lys Cys Ile Ser Ser Gln Lys Leu Ser Val Glu 200 Leu Val Gln Lys Trp Leu Ala Arg Tyr Met Phe Glu Asn Glu Ser Ala Ala Val Lys Lys Ser Lys Lys Ile Ser Glu Ile Met Ser Ser Ser Lys 235 230 Lys Tyr His Ser His Gly Arg Arg Ile Ser Arg Glu Glu Cys Lys Arg 250 Ile Gly Leu Lys Val Thr Asp Leu Glu Asp Glu Glu Phe Gln Asp 265 Leu Val Leu Ser Val Phe His Ala Ala Asn Thr Met Phe Gln Tyr Thr 280 Pro Val Asn Lys Ile Ile Met Asn His Leu Gly Asn Thr Val Val Glu

Thr Leu Pro Thr Pro Arg 305 310

<210> 45

<211> 1305

<212> DNA

<213> Cenarchaeum symbiosum

295

<220>

<221> CDS

<222> (1)...(1305)

<400> 45

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1				5					10				15	i	
													His	aac Asn	96
												Ala	_	ggc Gly	144
			-	_							gac Asp			atg Met	192
											cca Pro			_	240
_	_			_		-	_				ggg Gly		_		288
											gcg Ala				336
_	Glu	_				_	_	_		-	 gcc Ala 125	-	_		384
	_		_		_			_		-	ata Ile		_	_	432
											ctc Leu				480
											gtc Val				528
					_			_		_	 tcc Ser	_	_	_	576
											atc Ile 205				624
-	-				_		_	-	-	_	tat Tyr	_	_		672
											gtc Val				720

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										-			-	_	gca Ala	768
	ctg Leu	_		-												816
	ccc Pro					_		_	_			_	-			864
	act Thr 290		_		•	_		_								912
	ttc Phe		-			-	_	_					_			960
	gag Glu			_	_	_					_					1008
	ggg ggg		-													1056
_	tcc Ser						_	_		_				_		1104
	ggc Gly 370	_			_							_	-	-	_	1152
_	gag Glu	_	_					-	_	_				_		1200
	ttc Phe										_					1248
	gcc Ala											-		-	_	1296
	cta Leu	tga *														1305
		10>														

<211> 434

<212> PRT

<213> Cenarchaeum symbiosum

<400> 46

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	Phe	Ala	Ara	_	Lvs	Lvs	Tvr	His		เลา	Glv	. Val	Ser		Asn
			20	002	-7.5	_,_	-1-	25	• • • • • • • • • • • • • • • • • • • •	,	01,	-	30	****	
Ile	Arg	Phe		Glu	Pro	Tyr	Pro		Val	Thr	Arg	Ser		Ser	Gly
	_	35	_			-	40					45			•
Lys	His 50	Leu	Val	Asp	Val	Asp 55	Gly	Asn	Lys	Tyr	Val	Asp	Tyr	Trp	Met
Glv		Trp	Ser	Len	Tle		Glv	His	Ala	Pro		Pro	Val	Δτα	Sar
65					70		01,			75			•41	, m 9	80
Ala	Val	Glu	Gly	Gln	Leu	Arg	Arg	Gly	Trp	Ile	His	Gly	Thr	Val	
			_	85		_	_	_	90			_		95	
Glu	Gln	Thr	Met 100	Asn	Leu	Ser	Glu	Ile 105	Ile	Arg	Gly	Ala	Val 110	Ser	Val
Ala	Glu	Lys	Thr	Arg	Tyr	Val	Thr	Ser	Gly	Thr	Glu	Ala		Met	Tyr
		115			_		120		_			125			-
Ala	Ala	Arg	Leu	Ala	Arg	Ala	His	Thr	Gly	Arg	Lys	Ile	Ile	Ala	Lys
	130	_				135					140				
	Asp	Gly	Gly	Trp		Gly	Tyr	Ala	Ser	Gly	Leu	Leu	Lys	Ser	
145	M	D	m	7	150	D	~ 3	C	~ 1	155	•	**- 1			160
MSII	пр	PIO	IŅI	165	Val	PIO	GIU	ser	170	Gly	Leu	vaı	Asp	175	GIu
His	Ser	Ile	Ser		Pro	Tvr	Asn	Asp		Glu	Glv	Ser	I.em		Val
			180			-1-		185			1		190		
Leu	Gly	Arg	Ala	Gly	Asp	Asp	Leu	Ala	Cys	Val	Ile	Ile	Glu	Pro	Leu
		195					200					205			
Leu	Gly 210	Gly	Gly	Gly	Сув	Ile 215	Pro	Ala	Asp	Glu	Asp 220	Tyr	Leu	Arg	Gly
Ile	Gln	Glu	Phe	Val	His	Ser	Arg	Gly	Ala	Leu	Leu	Val	Leu	Asp	Glu
225					230				•	235					240
Ile	Val	Thr	Gly	Phe 245	Arg	Phe	Arg	Phe	Gly 250	Cys	Ala	Tyr	Ala	Ala 255	Ala
Gly	Leu	Asp	Pro 260	Asp	Ile	Val	Ala	Leu 265	Gly	Lys	Ile	Val	Gly 270	Gly	Gly
Phe	Pro	Ile 275	Gly	Val	Ile	Сув	Gly 280	Lys	Asp	Glu	Val	Met 285	Glu	Ile	Ser
Asn	Thr	Ile	Ser	His	Ala	Lys	Ser	Asp	Arg	Ala	Tyr	Ile	Gly	Gly	Gly
	290					295					300				
	Phe	Ser	Ala	Asn		Ala	Thr	Met	Thr	Ala	Gly	Ala	Ala	Ala	
305 Glv	Gl 11	Levi	Luc	Laze	310	Tve	Gl v	ም ኮ ~	Tla	315 Tyr	Dro	7 ~~~	T10	N ===	320
GIY	GIU	beu	цуз	325	Ary	цуs	GIY	1111	330	TYL	PIO	Arg	116	335	ser
Met	Gly	qeA	Asp 340		Arg	Asp	Lys	Leu 345		Lys	Ile	Phe	Gly 350		Arg
Val	Ser	Val		Glv	Arg	Glv	Ser		Phe	Met	Thr	His		Val	Gln
		355		,	5	,	360					365		•	
Asp	Gly	Ala	Gly	Arg	Val	Ser	Asn	Ala	Ala	Asp	Ala		Ala	Cys	Asp
	370					375					380			-	-
Val	Glu	Leu	Leu	His	Arg	Tyr	His	Leu	Asp	Met	Ile	Thr	Arg	Asp	Gly
385					390					395					400
Ile	Phe	Phe	Leu		Gly	Lys	Leu			Ile	Scr	Ala	Ala		Ser
T 1	- 1 ת	7	T a	405	mb	N/	m		410	0 -	~1		5 1	415	
		asp	Leu 420	ràs	ınr	мес		Ser 425	Ala	Ser	Glu		Phe 430	Ala	Glu '
Gly	Leu					•									

<210> 47 <211> 807

<212> DNA

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<213> Cenarchaeum symbiosum

<220> <221> CDS

<222> (1)...(807)

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											ata Ile	_	_		96	
											gtc Val 45				144	
_		_	_	_		_		_			gat Asp			_	192	
-		_		-			_		_	_	gcg Ala				240	
											acg Thr				288	
_	-				 _			_	_	_	cgg Arg			_	336	
											ggc Gly 125				384	
											gac Asp				432	
											aag Lys				480	
cac His											aag Lys				528	
ggc Gly											ctt Leu				576	
ggc Gly															624	

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cac His	c cgc Arg 210	g Glu	j aad 1 Asr	gce Ala	c aat a Asr	gta Val 215	l Let	g tat ı Tyı	geo Ala	c agg	g gcg g Ala 220	a Ar	c age	c cto	c tcg u Ser	672
ggc Gly 225	Leu	ggc Gly	agg Arg	gag Glu	g gad 1 Asp 230	Glı	tco Sei	ata Ile	gcg Ala	His 235	E Lev	g caa	a aaq n Lys	g gcg s Ala	g gcc a Ala 240	720
aaa Lys	aaa Lys	gat Asp	tcc Ser	Lys 245	Thr	ata Ile	aaa Lys	aag Lys	tgg Trp 250	Ala	cgo Arg	gca Ala	gaa Glu	aag Lys 255	g gcc s Ala	768
				Arg	gac Asp				Ser				Ī			807
	< <	210> 211> 212> 213>	268 PRT	arch	aeum	sym	bios	um								
	<-	400>	48													
Met 1	Ile	Leu	Phe	Gly 5	Lys	Ser	Asp	Pro	Ala 10	Glu	Leu	Val	Arg	Gln 15	Ala	
Asp	Leu	Leu	Cys 20	Ser	Lys	Asn	Gln	Phe 25	Arg	Ala	Ala	Ile	Gly 30	Leu	Tyr	
Gly	Lys	Ile 35	Leu	Lys	Asp	Asp	Pro		Asn	Arg	Gly	Val		His	Lys	
Lys	Gly 50	Leu	Ala	Gln	Asn	Arg 55	Ala	Lys	Lys	Tyr	Ser 60	Asp	Ala	Ile	Thr	
Cys 65	Phe	Asp	Arg	Leu	Leu 70	Glu	Leu	Asp	Asn	Lys 75	Asp	Ala	Pro	Ala	Tyr 80	
	Asn	Lys	Ala	Ile 85	Ala	Gln	Ala	Glu	Leu 90		Asp	Thr	Ala	Ser 95		
Leu	Glu	Asn	Tyr 100		Arg	Ala	Ile	Glu 105		Asp	Pro	Arg	Tyr 110		Pro	
Ala	Arg	Phe 115		Arg	Ala	Val	Leu 120		Asp	Arg	Leu			His	Glu	
Glu	Ala 130		Pro	Asp	Leu			Ala	Ala	Glu		125 Asp	Arg	Arg	Lys	
		Pro	Arg	Phe	Tyr	135 Lys	Gly	Ile	Val		140 Gly	Lys	Met	Gly	Arg	
145 His	Glu	Glu	Ala	Leu	150 Ala	Cys	Phe	Lys	Glγ	155 Val	Cvs	Lvs	Arq	His	160 Pro	
				165	Gln				170					175		
			180					185					190			
		195			Ala		200					205				
	210					215					220					
Gly 225	Leu	Gly	Arg	Glu	Asp 230	Glu	Ser	Ile		His 235	Leu	Gln	Lys	Ala		
	Lys	Asp		Lys 245	Thr	Ile	Lys				Arg	Ala		-	240 Ala	
Phe	Asp				Asp .	Asp	Pro			Lys	Arg			255		

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<210> 49 <211> 708 <212> DNA <213> Cenarchaeum symbiosum <220> <221> CDS <222> (1) ... (708) <400> 49 gtg cgg cag ggg atg act gga aag acc agg acg gcg gtc ctg cgg aac 48 Met Arg Gln Gly Met Thr Gly Lys Thr Arg Thr Ala Val Leu Arg Asn gcc atg act gag gag tcg gct cgg gcc atg ata gag gca aag aag acg 96 Ala Met Thr Glu Glu Ser Ala Arg Ala Met Ile Glu Ala Lys Lys Thr ggt gcc ttt agg gcc ctt atg agg gcc ccg cgg aaa gac gtc cat 144 Gly Ala Phe Arg Ala Leu Met Arg Ala Pro Arg Lys Glu Asp Val His 40 gtg cat tet gta aag etg gte cae gag geg etg ate egg gte tee gee 192 Val His Ser Val Lys Leu Val His Glu Ala Leu Ile Arg Val Ser Ala 50 agg tac tet geg gat ttt tte aga aag geg gtt cae eeg ate aag gtg Arg Tyr Ser Ala Asp Phe Phe Arg Lys Ala Val His Pro Ile Lys Val 65 70 gac cag aac gtg atc gag gtg gtg cta ggc gac ggc gtc ttt ccc ata 288 Asp Gln Asn Val Ile Glu Val Val Leu Gly Asp Gly Val Phe Pro Ile agg tcc aag tcg cgc ata cac aag acg ctc tcg gca ggg ctc ggc aag 336 Arg Ser Lys Ser Arg Ile His Lys Thr Leu Ser Ala Gly Leu Gly Lys 100 105 aac agg gtc gac ctc gag cta gaa gag cat gtc ttt gcg gaa tca gaa 384 Asn Arg Val Asp Leu Glu Leu Glu Glu His Val Phe Ala Glu Ser Glu 120 ggg atg atg tgc ctt gac cgg cac ggc ggc gag acg gac ttt ccc tac 432 Gly Met Met Cys Leu Asp Arg His Gly Gly Glu Thr Asp Phe Pro Tyr 135 aag acg ggg ccc ggc gcg gtg gag ccg tac ccg cgg agg ata ctc gat 480 Lys Thr Gly Pro Gly Ala Val Glu Pro Tyr Pro Arg Arg Ile Leu Asp 145 150 160 gcg tca gag aat gtg cgg agc ccc gag gtg gag aca gaa gag gcg ctc 528 Ala Ser Glu Asn Val Arg Ser Pro Glu Val Glu Thr Glu Glu Ala Leu 165 170 tca aaa cta aaa gag aag ctg cgc ggg ccc ccg cct gac ggc atg cgc 576 Ser Lys Leu Lys Glu Lys Leu Arg Gly Pro Pro Pro Asp Gly Met Arg 180 185

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gac ctg cgg gag gag ttt gcc gca aag gcg gtg gag gtg gtc tat gta 624 Asp Leu Arg Glu Glu Phe Ala Ala Lys Ala Val Glu Val Val Tyr Val 195 200 cca gtc tat gaa tcg cga ctt gtg ggg ccc aaa aaa aag gtc cgc atg 672 Pro Val Tyr Glu Ser Arg Leu Val Gly Pro Lys Lys Val Arg Met 210 atg cgg att gac gcg gca aga aaa aag atc ctc tag 708 Met Arg Ile Asp Ala Ala Arg Lys Lys Ile Leu * 230 <210> 50 <211> 235 <212> PRT <213> Cenarchaeum symbiosum <400> 50 Met Arg Gln Gly Met Thr Gly Lys Thr Arg Thr Ala Val Leu Arg Asn 5 10 Ala Met Thr Glu Glu Ser Ala Arg Ala Met Ile Glu Ala Lys Lys Thr 25 Gly Ala Phe Arg Ala Leu Met Arg Ala Pro Arg Lys Glu Asp Val His Val His Ser Val Lys Leu Val His Glu Ala Leu Ile Arg Val Ser Ala 55 Arg Tyr Ser Ala Asp Phe Phe Arg Lys Ala Val His Pro Ile Lys Val 70 75 Asp Gln Asn Val Ile Glu Val Val Leu Gly Asp Gly Val Phe Pro Ile 85 90 Arg Ser Lys Ser Arg Ile His Lys Thr Leu Ser Ala Gly Leu Gly Lys 105 Asn Arg Val Asp Leu Glu Leu Glu Glu His Val Phe Ala Glu Ser Glu 120 Gly Met Met Cys Leu Asp Arg His Gly Gly Glu Thr Asp Phe Pro Tyr 135 Lys Thr Gly Pro Gly Ala Val Glu Pro Tyr Pro Arg Arg Ile Leu Asp 150 155 Ala Ser Glu Asn Val Arg Ser Pro Glu Val Glu Thr Glu Glu Ala Leu 170 Ser Lys Leu Lys Glu Lys Leu Arg Gly Pro Pro Pro Asp Gly Met Arg 180 185 Asp Leu Arg Glu Glu Phe Ala Ala Lys Ala Val Glu Val Val Tyr Val 200 Pro Val Tyr Glu Ser Arg Leu Val Gly Pro Lys Lys Val Arg Met 215 Met Arg Ile Asp Ala Ala Arg Lys Lys Ile Leu 230 <210> 51 <211> 378 <212> DNA <213> Cenarchaeum symbiosum

<220> <221> CDS

<222> (1)...(378)

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_				5					10					15		
															gca	96
Ala	qaA	Lys		Ile	Asp	Asn	Ala		Glu	Gln	Gly	Val		Arg	Ala	
			20					25					30			
gac	gag	ata	cta	gat	gac	qca	gtc	gag	ctc	ggc	aag	atc	acc	gtg	ggc	144
															Gly	
		35					40					45				
aaa	gcg	caa	222	aga	age	gat	ata	cta	ctc	aaq	cao	acc	gag	caa	gag	192
															Glu	-72
	50		-	-		55			•		60					
					.			~~~		226	ata	~~~	224			240
	aag Lys															240
65	-7-	5		-1-	70	3	2			75			4	1	80	
	gcg Ala															288
GIY	Ala	AIa	БУЗ	B5	Mec	AIA	AIG	GIY	90	Gly	ഹാ	AIG	Deu	95	1111	
	gca															336
Leu	Ala	Lys	Leu 100	GIY	Glu	Leu	Arg	Lys 105	Ala	GIY	TIE	тте	110	GIu	гàг	
			100					103								
	ttt												tga			378
Glu	Phe	_	Ala	Lys	Lys	Lys		Leu	Leu	Ala	Glu		*			
		115					120					125				
	<2	210>	52													
		211>														
		112>		rchs	Allm	symb	ni osi	ım								
	~2	.137	Cerre	ii Cile	ieum	Syllin	,1080	4111								
		<00>	-													
	Arg	Ser	Glu	Gly	Arg	Pro	Gly	Tyr	Ile 10	Glu	Lys	Phe	Leu	Lys	Arg	
l Ala	Asp	Lvs	Ala	Ile	Asp	Asn	Ala	Val		Gln	Glv	Val	Lvs	Ara	Ala	
		-10	20					25			2		30	5		
Asp	Glu	Ile	Leu	qaA	qaA	Ala		Glu	Leu	Gly	Lys		Thr	Val	Gly	
0 7	.1-	35	•	•		>	40	T	T	T	a 1	45	a 1	3	01	
GIU	Ala 50	GIN	гàг	Arg	ser	Asp 55	vai	Leu	ren	гуя	60	Ala	GIU.	Arg	GIU	
Ser	Lys	Arg	Leu	Lys	Ser		Gly	Ala	Lys	Lys	Leu	Glu	Lys	Gly	Ile	
65	-	_		-	70	_	_		_	75				_	80	
Gly	Aļa	Ala	Lys	-	Met	Ala	Ala	Gly		Gly	Asp	Ala	Leu		Thr	
Len	Ala	Lve	וום, [85 Glv	Glu	Len	Ara	Lvs	90 Ala	Glv	Ile	Ile	Thr	95 Glu	Lvs	
204		-,-	100	 y	4		3	105		1			110		-,0	
Glu	Phe	Arg	Ala	Lys	Lys	Lys		Leu	Leu	Ala	Glu					
		115					120					125				

<210> 53 <211> 606 -105-

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195 200 <210> 54 <211> 201 <212> PRT <213> Cenarchaeum symbiosum Met Ser Lys Thr Glu Ala Ser Pro Gly Gly Tyr Ala Cys Thr Pro Tyr Thr His Asp His Ala Ser Ile Glu Leu Lys Glu Glu Trp Ser Ser Ser 25 Arg Asn Val Gly Glu Met Tyr Phe Val Thr Ala Thr Phe Ser Ser Lys 40 Ser Lys Pro Tyr Phe Glu Gln Gln Ala Ser His Tyr Leu Leu Ala Arg Phe Lys Asn Gly Pro Lys Met Ile Lys Ala Val Glu Gly Arg Gly Gly 70 75 Gly Pro Ser Tyr Leu Phe Ser Met Asp Glu Glu Ile Phe Glu Arg Glu Ser Pro Gly Met Ser Tyr Val Ser Met Tyr Tyr Leu Glu Tyr Gly Asp 105 Ser Glu Glu Asp Ile Arg Glu Val Ala Ser Val Val Ala Arg Lys Glu 120 Lys Ile Gly Arg Ala Gly Ile Gly Arg Met Asp Val Cys Ser Arg Ile 135 140 Pro Pro Lys Phe Ala Phe Pro Tyr Ser Gly Asn Ile Val Val Leu Glu 150 155 Val Ser Ser Glu Lys Ser His Gln Ser Val Asn Lys Tyr Cys Glu Lys 170 Thr Arg Arg Glu Val Ile Arg Lys Gly Ile Thr Met Thr Asn Leu Val 185 Ser Leu Ser Ile Leu Glu Arg Leu Lys 195 <210> 55 <211> 822 <212> DNA <213> Cenarchaeum symbiosum <220> <221> CDS <222> (1)...(822) <400> 55 ttg aaa agt acg ttg gtt cgg cgc tac aag ccc aag ata aag cag acc 48 Met Lys Ser Thr Leu Val Arg Arg Tyr Lys Pro Lys Ile Lys Gln Thr 5

ctc cgc gag gtg ccc ctc aaa aat gtg cat gtg tgg aag gag gcg cag
Leu Arg Glu Val Pro Leu Lys Asn Val His Val Trp Lys Glu Ala Gln
20 25 30

gca agg agg ctg gac agg tcc cgg gtg cgg gat atc gca aag tcg atc
Ala Arg Arg Leu Asp Arg Ser Arg Val Arg Asp Ile Ala Lys Ser Ile
35 40 45

aga toa gag ggg ctg cag aac ccg ccc gtc ata cag agg ggc ggc agg 192

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Arg	Ser 50		Gly	Leu	Gln	Asn 55	Pro	Pro	Val	Ile	Gln 60	_	Gly	Gly	Arg	
	Leu										Leu				aag Lys 80	240
										Val					aca Thr	288
			_	_	_	_	_	_	-		_	_			ctg Leu	336
												gca Ala 125				384
_	_		_	_					_	-		aag Lys			_	432
												ggc Gly		_	_	480
					-							gac Asp				528
												ctc Leu				576
	-		_	_		_		_	_			atc Ile 205		_		624
												ata Ile				672
												gag Glu	_		_	720
												gag Glu				768
		Arg										ctg Leu				816
cga Arg	tga *															822

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<210> 56 <211> 273

<212> PRT

<213> Cenarchaeum symbiosum

<400> 56 Met Lys Ser Thr Leu Val Arg Arg Tyr Lys Pro Lys Ile Lys Gln Thr 10 Leu Arg Glu Val Pro Leu Lys Asn Val His Val Trp Lys Glu Ala Gln 25 Ala Arg Arg Leu Asp Arg Ser Arg Val Arg Asp Ile Ala Lys Ser Ile 40 Arg Ser Glu Gly Leu Gln Asn Pro Pro Val Ile Gln Arg Gly Gly Arg 55 Gly Leu Tyr Leu Leu Ile Ser Gly His His Arg Leu Ala Ala Leu Lys Tyr Leu Gly Ala Lys Lys Ser Lys Phe Leu Val Ile Thr Lys Asp Thr Glu Tyr Gly Leu Asp Asp Ala Lys Ala Ala Ser Val Val Glu Asn Leu 105 His Arg Leu Gln Met Ser Pro Arg Glu Leu Ala Asp Ala Cys Lys Phe 120 Leu Ala Glu Gln Thr Thr Lys Ser Glu Ala Ala Lys Lys Leu Gly Met 135 Ser Met Pro Thr Phe Lys Lys Tyr His Gly Phe Ala Gly Val Pro Asp 150 155 Lys Ile Lys Ala Met Val Pro Gly Thr Ile Ser Arg Asp Glu Ala Thr 170 Arg Leu Tyr Gln Ala Val Pro Thr Ile Ser Gln Ala Leu Lys Val Val 180 185 Ser Lys Ile Ala Lys Leu Asp Arg Pro Ser Arg Arg Ile Tyr Leu Arg 200

Leu Leu Ala Gln Ser Pro Arg Ser Gly His Lys Ile Ile Leu Lys Arg 210 215 220

Met Arg Lys Val Gly Ile Lys Lys Ile Pro Ile Glu Leu Gly Lys 225 230 235 240

Asn Gly Ala Arg Lys Leu Ser Arg Leu Ala Glu Arg Glu Gly Thr Asp 245 250 255

Glu Thr Arg Leu Ala Asn Arg Ile Val Arg Glu Tyr Leu Arg Lys Arg
260 265 270

Arg

<210> 57

<211> 669

<212> DNA

<213> Cenarchaeum symbiosum

<220>

<221> CDS

<222> (1)...(669)

<400> 57

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Met Ala Arg Ser Pro Val Leu Ile Ile Asn Cys Lys Asn Tyr Lys Glu
1 5 10 15

gcg gcc ggc ggc aga att gac agc cta gcg gcg gca gcc gcc ggg gcg 96 Ala Ala Gly Gly Arg Ile Asp Ser Leu Ala Ala Ala Ala Ala Gly Ala

			20					25					30)		
								Ala					Gln		Leu Leu	144
			_								ctg Leu 60		_		ata Ile	192
											gtc Val					240
											aac Asn		_	_		288
											ccc Pro					336
											tcc Ser					384
											atc Ile 140					432
											agg Arg					480
											gga Gly					528
tgc Cys	gly aaa	Ala	ggc Gly 180	ata Ile	aca Thr	tca Ser	ggc Gly	gct Ala 185	gat Asp	gtg Val	cgc Arg	aag Lys	gcc Ala 190	ctc Leu	gag Glu	576
											gtg Val					624
				_		-		_	_	_	gcc Ala 220	_		tga *		669
	<2 <2	10> 11> 12> 13>	222 PRT	rcha	eum	symb	iosu	m								
						7			•							
Met 1		00> Arg		Pro	Val	Leu	Ile		Asn 10	Cys	Lys	Asn	-	Lys 15	Glu	

10

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Ala Ala Gly Gly Arg Ile Asp Ser Leu Ala Ala Ala Ala Gly Ala Ala Ala Lys Tyr Gly Val Arg Ile Ala Leu Ala Pro Pro Gln His Leu 40 Leu Gly Ala Val Lys Gly Glu Asp Leu Thr Val Leu Ala Gln His Ile 55 Asp Asp Lys Gly Val Gly Ser Thr Thr Gly Tyr Val Val Pro Glu Leu 70 75 Leu Gly Glu Ser Gly Val Ser Gly Ala Leu Ile Asn His Ser Glu His 85 90 Arg Val Ser Ala Asp Gln Val Ala Ser Leu Val Pro Arg Leu Arg Gly Leu Asp Met Ile Ser Val Val Cys Val Lys Asp Ser Ala Glu Ala Ala 120 Asn Leu Ser Arg His Arg Pro Asp Tyr Ile Ala Ile Glu Pro Pro Glu 135 Leu Ile Gly Ser Gly Arg Ser Val Ser Ser Glu Arg Pro Glu Leu Ile 150 155 Gly Glu Ala Ala Glu Ala Ile Arg Gly Ala Asp Gly Thr Lys Leu Leu 170 165 Cys Gly Ala Gly Ile Thr Ser Gly Ala Asp Val Arg Lys Ala Leu Glu 185 Leu Gly Ser Lys Gly Ile Leu Val Ala Ser Gly Val Val Lys Ser Ser 200 205 Asp Pro Ala Ala Ile Ala Glu Leu Ala Gln Ala Met Ser 215 <210> 59 <211> 549 <212> DNA <213> Cenarchaeum symbiosum · <220> <221> CDS <222> (1)...(548) <400> 59 atg ctg gat ccc cgg acg cgc ccc cgg gtc gtc aat gtc gtc agc aca Met Leu Asp Pro Arg Thr Arg Pro Arg Val Val Asn Val Val Ser Thr tca gac ctt gta caa agg gtg agc gca aaa aag atg gcc gcc atg ccg 96 Ser Asp Leu Val Gln Arg Val Ser Ala Lys Lys Met Ala Ala Met Pro 20 tgc tgc atg tat gat gag gcc gta tac ggc ggc agg tgc ggc tac ata 144 Cys Cys Met Tyr Asp Glu Ala Val Tyr Gly Gly Arg Cys Gly Tyr Ile aag acg ccc ggc atg cag ggg agg gtg act gta ttc att tct ggc aag 192 Lys Thr Pro Gly Met Gln Gly Arg Val Thr Val Phe Ile Ser Gly Lys 55 atg ata tee gte gge gee aga tee gtg agg gee teg ttt ggg cag etg 240 Met Ile Ser Val Gly Ala Arg Ser Val Arg Ala Ser Phe Gly Gln Leu 70 75 cac gag gcg cgg ctc cac ctg gtg cgc aac ggg gct gcc ggc gac tgc 288

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His Glu Ala Arg Leu His Leu Val Arg Asn Gly Ala Ala Gly Asp Cys aag ata agg ccc gtc gtg cgc aat att gta gcc acg gtg gat gcc ggt 336 Lys Ile Arg Pro Val Val Arg Asn Ile Val Ala Thr Val Asp Ala Gly 105 100 agg aat gtt ccc ata gac agg ata tcg tcg cgc atg cct ggc gct gta 384 Arg Asn Val Pro Ile Asp Arg Ile Ser Ser Arg Met Pro Gly Ala Val 120 115 tat gat ecc ggg teg ttt ecc ggg atg ata etc aag ggg etg gac age 432 Tyr Asp Pro Gly Ser Phe Pro Gly Met Ile Leu Lys Gly Leu Asp Ser 135 130 tgc agc ttt cta gtc ttt gcg tcg gga aag atg gtg ata gcg ggc gcc 480 Cys Ser Phe Leu Val Phe Ala Ser Gly Lys Met Val Ile Ala Gly Ala aag tog cog gat gag ctg cgc agg tog tog ttt gac ctg ctg acg cgc 528 Lys Ser Pro Asp Glu Leu Arg Arg Ser Ser Phe Asp Leu Leu Thr Arg 170 165 549 ctc aat aac gcg ggg gcc ta g Leu Asn Asn Ala Gly Ala 180 <210> 60 <211> 182 <212> PRT <213> Cenarchaeum symbiosum <400> 60 Met Leu Asp Pro Arg Thr Arg Pro Arg Val Val Asn Val Val Ser Thr 10 5 Ser Asp Leu Val Gln Arg Val Ser Ala Lys Lys Met Ala Ala Met Pro 25 Cys Cys Met Tyr Asp Glu Ala Val Tyr Gly Gly Arg Cys Gly Tyr Ile 40 Lys Thr Pro Gly Met Gln Gly Arg Val Thr Val Phe Ile Ser Gly Lys 60 55 Met Ile Ser Val Gly Ala Arg Ser Val Arg Ala Ser Phe Gly Gln Leu 75 70 His Glu Ala Arg Leu His Leu Val Arg Asn Gly Ala Ala Gly Asp Cys 90 85 Lys Ile Arg Pro Val Val Arg Asn Ile Val Ala Thr Val Asp Ala Gly 105 Arg Asn Val Pro Ile Asp Arg Ile Ser Ser Arg Met Pro Gly Ala Val 120 Tyr Asp Pro Gly Ser Phe Pro Gly Met Ile Leu Lys Gly Leu Asp Ser 140 135 Cys Ser Phe Leu Val Phe Ala Ser Gly Lys Met Val Ile Ala Gly Ala 155 150 Lys Ser Pro Asp Glu Leu Arg Arg Ser Ser Phe Asp Leu Leu Thr Arg 170 165 Leu Asn Asn Ala Gly Ala

180

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<210> 61 <211> 2538 <212> DNA <213> Cenarchaeum symbiosum <220> <221> CDS <222> (1)...(2538) <400> 61 ctg act gca cag gat gaa gag att ccc ccg tca ctg ctt gta tct gca 48 Met Thr Ala Gln Asp Glu Glu Ile Pro Pro Ser Leu Leu Val Ser Ala 10 acc tat gat ggc cag gca agg gcc gtg gtc ctc aag ttc tac gag tcg 96 Thr Tyr Asp Gly Gln Ala Arg Ala Val Leu Lys Phe Tyr Glu Ser gaa tog caa aag ato ato cac tgg acg gac aac acg ggg cac aag coc 144 Glu Ser Gln Lys Ile Ile His Trp Thr Asp Asn Thr Gly His Lys Pro 40 tac tgt tat acg agg ctg ccg ccc tcc gag ctc ggc ttt ctt ggg ggc 192 Tyr Cys Tyr Thr Arg Leu Pro Pro Ser Glu Leu Gly Phe Leu Gly Gly 50 55 60 agg gag gac gtg ctc ggg ata gag cag gtc atg cgg cac gac ctg ata 240 Arg Glu Asp Val Leu Gly Ile Glu Gln Val Met Arg His Asp Leu Ile gec gac aag gag gtg eec gte tee aag ata acc gte tet gat eet ett 288 Ala Asp Lys Glu Val Pro Val Ser Lys Ile Thr Val Ser Asp Pro Leu gcg ata ggc ggg acc cac tcg gag aag agc atc aga aac gtg ata gac 336 Ala Ile Gly Gly Thr His Ser Glu Lys Ser Ile Arg Asn Val Ile Asp 100 105 acg tgg gaa tcc gac ata aag tat tac gag aac tat ctg tat gac gcg 384 Thr Trp Glu Ser Asp Ile Lys Tyr Tyr Glu Asn Tyr Leu Tyr Asp Ala 115 120 ggc ctg gta gtg ggc agg tac tat tcg gta tca ggc ggg gag gtg att 432 Gly Leu Val Val Gly Arg Tyr Tyr Ser Val Ser Gly Gly Glu Val Ile ccg cat gac atg cca ata tcc gac gag gta aaa ctg gcc ctc aag agc 480 Pro His Asp Met Pro Ile Ser Asp Glu Val Lys Leu Ala Leu Lys Ser 145 150 ctt ctc tgg gac aag ctc ata gac gag ggc atg gcc gac agg aaa gag 528 Leu Leu Trp Asp Lys Leu Ile Asp Glu Gly Met Ala Asp Arg Lys Glu 165 170 175 ttc cgc gag ttc ata gcg ggg tgg gcg gac ctg ctc aac cag ccc ata 576 Phe Arg Glu Phe Ile Ala Gly Trp Ala Asp Leu Leu Asn Gln Pro Ile 180 185

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				_		_	Asp			 _	Ser		gag Glu	624
			•	_	_	_	_	_		 -		-	gtg	672
		_	_		_		_	_	_	_	_	_	agc Ser 240	720
	gcg Ala				_					 -				768
	tac Tyr												_	816
	ata Ile													864
_	atg Met 290	_		_			 _		-				_	912
	gac Asp													960
	gtc Val		_	-	_				_		_		_	1008
	tat Tyr	-			_	_		_		_		_		1056
	aag Lys													1104
	gat Asp 370													1152
	ctg Leu													1200
	ctg Leu						Ala							1248
	cgc Arg													1296

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		420	-			425				430			
	 _	Arg			-		_	 _		_	_	aag Lys	1344
									gac Asp				1392
_	 		_	_		_			cac His		-	_	1440
									ata Ile				1488
									gaa Glu				1536
									aaa Lys 525				1584
									cgc Arg				1632
									gag Glu	_		_	1680
									cta Leu				1728
									ttt Phe				1776
									atg Met 605				1824
				Met					GJA aaa				1872
									cat His				1920
		Lys				Val			gtg Val				1968

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	agg Arg		_						_							2016	
	aag Lys				_	-	_	_			_			_	_	2064	
	acg Thr 690															2112	
_	tcg Ser	_	_				_			_	_	_	_		_	2160	
	tca Ser															2208	
	ccg Pro											_	_			2256	
	gaa Glu												-	_	_	2304	
	gag Glu 770		_			_				_			_		_	2352	
	gtg Val											_	_	Gln	_	2400	
	gag Glu		Asp	_		-		Leu			_				_	2448	
	cag Gln	Leu					Gly					Glu				2496	
_	cca Pro	_	_			_							tga *			2538	
	<2	10>	62														

<211> 845

<212> PRT

<213> Cenarchaeum symbiosum

<400> 62

Met Thr Ala Gln Asp Glu Glu Ile Pro Pro Ser Leu Leu Val Ser Ala 1 5 5 5 10 10 5 15 Thr Tyr Asp Gly Gln Ala Arg Ala Val Val Leu Lys Phe Tyr Glu Ser 20 25 5 30 -116-

Glu Ser Gln Lys Ile Ile His Trp Thr Asp Asn Thr Gly His Lys Pro 40 Tyr Cys Tyr Thr Arg Leu Pro Pro Ser Glu Leu Gly Phe Leu Gly Gly Arg Glu Asp Val Leu Gly Ile Glu Gln Val Met Arg His Asp Leu Ile Ala Asp Lys Glu Val Pro Val Ser Lys Ile Thr Val Ser Asp Pro Leu 85 90 Ala Ile Gly Gly Thr His Ser Glu Lys Ser Ile Arg Asn Val Ile Asp 100 105 Thr Trp Glu Ser Asp Ile Lys Tyr Tyr Glu Asn Tyr Leu Tyr Asp Ala 120 Gly Leu Val Val Gly Arg Tyr Tyr Ser Val Ser Gly Gly Glu Val Ile 135 140 Pro His Asp Met Pro Ile Ser Asp Glu Val Lys Leu Ala Leu Lys Ser 150 155 Leu Leu Trp Asp Lys Leu Ile Asp Glu Gly Met Ala Asp Arg Lys Glu 170 Phe Arg Glu Phe Ile Ala Gly Trp Ala Asp Leu Leu Asn Gln Pro Ile 185 Pro Arg Ile Arg Arg Leu Ser Phe Asp Ile Glu Val Asp Ser Glu Glu 200 Gly Arg Ile Pro Asp Ala Lys Ile Ser Asp Arg Arg Val Thr Ala Val 215 220 Gly Phe Ala Ala Thr Asp Gly Leu Arg Lys Val Leu Val Leu Lys Ser 230 235 Gly Ala Asp Glu Gly Ala Asn Asp Val Thr Pro Gly Val Glu Val Val 245 250 Phe Tyr Asp Glu Asp Lys Glu Ala Asp Met Ile Arg Asp Ala Leu Ala 260 265 Ile Ile Gly Ser Tyr Pro Phe Val Leu Thr Tyr Asn Gly Asp Asp Phe 280 Asp Met Pro Tyr Met Tyr Asn Arg Ala Arg Arg Leu Gly Val Ala Asp 300 295 Ser Asp Ile Pro Leu Tyr Met Met Arg Asp Ser Ala Thr Leu Arg His 310 315 Gly Val His Leu Asp Leu Tyr Arg Thr Phe Ser Asn Arg Ser Phe Gln 325 330 Leu Tyr Ala Phe Ala Ala Lys Tyr Thr Asp Tyr Ser Leu Asn Ser Val 345 Ser Lys Ala Met Leu Gly Glu Gly Lys Val Asp Tyr Gly Val Ser Leu 360 365 Gly Asp Leu Thr Leu Tyr Gln Thr Ala Asn Tyr Cys Tyr His Asp Ala 375 380 Arg Leu Thr Leu Glu Leu Ser Thr Phe Gly Asn Glu Ile Leu Met Asp 395 390 Leu Leu Val Val Thr Ser Arg Ile Ala Arg Met Pro Ile Asp Asp Met 410 Ser Arg Met Gly Val Ser Gln Trp Ile Arg Ser Leu Leu Tyr Tyr Glu 425 His Arg Gln Arg Asn Ala Leu Ile Pro Arg Arg Asp Glu Leu Glu Lys 440 Arg Ser Gln Gln Val Ser Asn Asp Ala Val Ile Lys Asp Lys Lys Phe 455 Arg Gly Gly Leu Val Val Glu Pro Glu Glu Gly Ile His Phe Asp Val 470 475 Thr Val Met Asp Phe Ala Ser Leu Tyr Pro Ser Ile Ile Lys Val Arg 490 485

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```
Asn Leu Ser Tyr Glu Thr Val Arg Cys Val His Pro Glu Cys Arg Lys
                                505
Asn Thr Ile Pro Asp Thr Asn His Trp Val Cys Thr Lys Asn Asn Gly
                           520
Leu Thr Ser Met Ile Ile Gly Ser Leu Arg Asp Leu Arg Val Asn Tyr
                        535
Tyr Lys Ser Leu Ser Lys Ser Gln Ser Ile Thr Glu Glu Gln Arg Gln
                    550
                                       555
Gln Tyr Thr Val Ile Ser Gln Ala Leu Lys Val Val Leu Asn Ala Ser
                                   570
Tyr Gly Val Met Gly Ala Glu Ile Phe Pro Leu Tyr Phe Leu Pro Ala
                               585
Ala Glu Ala Thr Thr Ala Val Gly Arg Tyr Ile Ile Met Gln Thr Ile
                        600
Ser His Cys Glu Gln Met Gly Val Lys Val Leu Tyr Gly Asp Thr Asp
                       615
                                          620
Ser Leu Phe Ile Lys Asn Pro Glu Glu Arg Gln Ile His Asp Ile Val
Glu His Ala Lys Lys Glu His Gly Val Glu Leu Glu Val Asp Lys Glu
               645
                                   650
Tyr Arg Tyr Val Val Leu Ser Asn Arg Lys Lys Asn Tyr Phe Gly Val
                               665
Thr Lys Ser Gly Lys Val Asp Val Lys Gly Leu Thr Gly Lys Lys Ser
                          680
His Thr Pro Pro Phe Ile Lys Glu Leu Phe Tyr Ser Leu Leu Asp Ile
                       695
Leu Ser Ala Val Gln Thr Glu Asp Glu Phe Glu Ser Ala Lys Leu Lys
                   710
                                      715
Ile Ser Lys Ala Ile Ala Ala Ser Gly Lys Arg Leu Glu Glu Arg Gly
               725
Val Pro Leu Ala Asp Leu Ala Phe Asn Val Met Ile Ser Lys Ala Pro
           740
                              745
Ser Glu Tyr Val Lys Thr Val Pro Gln His Ile Arg Ala Ala Arg Leu
                           760
Leu Glu Asn Ala Arg Glu Val Lys Lys Gly Asp Ile Ile Ser Tyr Val
                       775
Lys Val Met Asn Lys Thr Gly Val Lys Pro Val Glu Met Ala Gln Ala
                   790
                                       795
Gly Glu Val Asp Thr Ser Lys Tyr Leu Glu Phe Met Glu Ser Thr Leu
                                   810
Asp Gln Leu Thr Ser Ser Met Gly Leu Asp Phe Asp Glu Met Leu Gly
                              825
Lys Pro Lys Gln Thr Gly Met Glu Gln Phe Phe Lys
       835
                           840
     <210> 63
     <211> 642
     <212> DNA
     <213> Cenarchaeum symbiosum
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<220>

<221> CDS

<222> (1) ... (642)

<400> 63

ttg ccc gtt atg tgt gcg gtc tcc acg cgc ggc cct gac gcg gcc tgt
Met Pro Val Met Cys Ala Val Ser Thr Arg Gly Pro Asp Ala Ala Cys

1 10 15

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				Ser					Tyr					Arg	gcg Ala	96
			Trp	_	-						-			_	gaa Glu	144
		Met	_	_								tcc Ser		_	_	192
	_	_			_	-		_		_		agg Arg	_	_	_	240
												tgc Cys				288
	_	-		-			_	_			_	atc Ile	_			336
		_	_		_	_	_			_		gcc Ala 125				384
		_			_				_			ggc Gly		-		432
												aag Lys				480
							_	_	_	-		tat Tyr	-			528
												acc Thr			-	576
_		_				Trp					Pro	ggg Gly 205	Gly		_	624
gag Glu		-		_	tga *											642

<210> 64

<211> 213

<212> PRT

<213> Cenarchaeum symbiosum

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<400> 64 Met Pro Val Met Cys Ala Val Ser Thr Arg Gly Pro Asp Ala Ala Cys Cys Phe Met Val Ser Tyr Thr Gly Ala Tyr Thr Ile Ile Cys Arg Ala Val Ala Pro Trp Pro Leu Ser Gly Phe Glu Arg Pro Ser Trp Asp Glu 40 Tyr Phe Met Leu Gln Ala Glu Leu Ala Lys Leu Arg Ser Asn Cys Met 55 Val Arg Lys Val Gly Ala Val Ile Val Arg Asp His Arg Gln Leu Ala Thr Gly Tyr Asn Gly Thr Pro Pro Gly Val Lys Asn Cys Phe Glu Gly 85 90 Gly Cys Glu Arg Cys Ile Glu Arg Met Glu Gly Lys Ile Arg Ser Gly 105 Glu Gly Leu Asp Arg Cys Leu Cys Asn His Ala Glu Ala Asn Ala Ile 120 Met His Cys Ala Ile Leu Gly Ile Gly Ala Gly Gly Asn Ala Thr 135 140 Met Tyr Thr Thr Phe Ser Pro Cys Leu Glu Cys Thr Lys Met Ala Val 150 155 Thr Ile Gly Ile Arg Arg Phe Val Cys Leu Asp Thr Tyr Pro Glu Asn 165 170 Ala Ser Lys Leu Val Lys Asp Ala Ser Ala Ser Ile Thr Met Met Asp 185 Lys Glu Lys Ile Thr Tyr Trp Ala Ser Arg Met Pro Gly Gly Thr Lys 195 200 205 Glu Val Pro Val Arg 210 <210> 65 <211> 1512 <212> DNA <213> Cenarchaeum symbiosum <220> <221> CDS <222> (1)...(1512) <400> 65 gtg gag acc gca cac ata acg ggc aaa tac gta gag ccc ggc gcc gtc 48 Met Glu Thr Ala His Ile Thr Gly Lys Tyr Val Glu Pro Gly Ala Val gag agg cgc gac tac cag gtg ggc ctt gcc gag cag gcc ata cgg gaa 96 Glu Arg Arg Asp Tyr Gln Val Gly Leu Ala Glu Gln Ala Ile Arg Glu aac tgc ata gtg gtg ctg cct acc ggc ctc ggc aag acg gcc gtg gcc 144 Asn Cys Ile Val Val Leu Pro Thr Gly Leu Gly Lys Thr Ala Val Ala 35 40 ctg cag gtg atc tcc cac tat ttg gac gaa ggc agg ggg gct ctc ttc 192 Leu Gln Val Ile Ser His Tyr Leu Asp Glu Gly Arg Gly Ala Leu Phe `50 55 ctt gcg ccg aca agg gtg ctg gta aac cag cac cgc cag ttc ctg ggc 240 Leu Ala Pro Thr Arg Val Leu Val Asn Gln His Arg Gln Phe Leu Gly

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65	i				70					75					80		
					Ser					Val					acc Thr	2	88
				Lys							-			Ala	acc		36
			Thr		aac Asn								Pro			3	84
					gtg Val							Ala				4	32
					ata Ile 150											41	80
					acc Thr											52	28
					ctc Leu											`5 7	76
					ccc Pro											62	24
Lys	Val 210	Glu	Leu	Pro	ccg Pro	Glu 215	Met.	Lys	Glu	Ile	Gln 220	Lys	Leu	Leu	Lys	67	72
Met 225	Ala	Leu	Asp	Glu	aga Arg 230	Tyr	Ala	Ala	Leu	Lys 235	Arg	Cys	Gly	Tyr	Asp 240	72	20
					tcg Ser											76	8
					agg Arg											81	.6
					ctc Leu	Asn										86	4
					gag Glu					Lys						91	2

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	Glu					Asp					Gly				cgc Arg 320	960
						gcc Ala									aag Lys	1008
_	-		_		_	ggg Gly	_			_		_	_			1056
-			_		_	gat Asp					-	_	_	_	_	1104
			_			ctc Leu 375			_		_	-	_			1152
_	-			_	_	gag Glu		_	-	_		_	_			1200
						aca Thr										1248
-		-				gta Val			_		-		_	_		1296
						ggc Gly										1344
_		_	_	-	~	aag Lys 455				_		-				1392
			_	_		act Thr	_	_	Arg		_		_		-	1440
	_	_		_		ggg Gly					_	_	Ala			1488
aag Lys						ttc Phe	tag *									1512

<210> 66

<211> 503

<212> PRT

<213> Cenarchaeum symbiosum

<400> 66

Met Glu Thr Ala His Ile Thr Gly Lys Tyr Val Glu Pro Gly Ala Val Glu Arg Arg Asp Tyr Gln Val Gly Leu Ala Glu Gln Ala Ile Arg Glu 25 Asn Cys Ile Val Val Leu Pro Thr Gly Leu Gly Lys Thr Ala Val Ala Leu Gln Val Ile Ser His Tyr Leu Asp Glu Gly Arg Gly Ala Leu Phe 55 Leu Ala Pro Thr Arg Val Leu Val Asn Gln His Arg Gln Phe Leu Gly 70 75 Arg Ala Leu Thr Ile Ser Asp Ile Thr Leu Val Thr Gly Glu Asp Thr 90 Val Pro Arg Arg Lys Lys Ala Trp Gly Gly Ser Val Ile Cys Ala Thr 100 105 Pro Glu Ile Thr Arg Asn Asp Ile Ala Arg Gly Met Val Pro Leu Glu 120 Gln Phe Gly Leu Val Val Phe Asp Glu Ala His Arg Ala Val Gly Asp 135 Tyr Ala Tyr Ser Ala Ile Ala Arg Ala Val Gly Glu Asn Ser Arg Met 150 155 Ile Gly Met Thr Ala Thr Leu Pro Ser Glu Arg Glu Lys Ala Asp Glu 165 170 Ile Met Gly Thr Leu Leu Ser Lys Ser Ile Ala Gln Arg Thr Glu Asp 180 185 Asp Pro Asp Val Lys Pro Tyr Val Glu Glu Thr Glu Thr Glu Trp Ile 200 205 Lys Val Glu Leu Pro Pro Glu Met Lys Glu Ile Gln Lys Leu Leu Lys 215 Met Ala Leu Asp Glu Arg Tyr Ala Ala Leu Lys Arg Cys Gly Tyr Asp 230 235 Leu Gly Ser Asn Arg Ser Leu Ser Ala Leu Leu Arg Leu Arg Met Val 250 Val Leu Ser Gly Asn Arg Arg Ala Ala Lys Pro Leu Phe Thr Ala Ile 265 Arg Ile Thr Tyr Ala Leu Asn Ile Phe Glu Ala His Gly Val Thr Pro 280 Phe Leu Lys Phe Cys Glu Arg Thr Val Lys Lys Gly Ala Gly Val 295 300 Ala Glu Leu Phe Glu Glu Asp Arg Asn Phe Thr Gly Ala Met Ala Arg 310 315 Ala Lys Ala Ala Gln Ala Ala Gly Met Glu His Pro Lys Ile Pro Lys 325 330 Leu Glu Glu Ala Val Arg Gly Ala Lys Gly Lys Ala Leu Val Phe Thr 345 Ser Tyr Arg Asp Ser Val Asp Leu Ile His Ser Lys Leu Gln Ala Ala 360 Gly Ile Asn Ser Gly Ile Leu Ile Gly Lys Ala Gly Glu Lys Gly Leu 375 380 Lys Gln Lys Lys Gln Val Glu Thr Val Ala Lys Phe Arg Asp Gly Gly 390 395 Tyr Asp Val Leu Val Ser Thr Arg Val Gly Glu Gly Leu Asp Ile 405 410 Ser Glu Val Asn Leu Val Val Phe Tyr Asp Asn Val Pro Ser Ser Ile 425 Arg Tyr Val Gln Arg Arg Gly Arg Thr Gly Arg Lys Asp Ala Gly Lys 440 Leu Val Val Leu Met Ala Lys Gly Thr Ile Asp Glu Ala Tyr Tyr Trp 460

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Ile Gly Arg Arg Lys Ile Thr Ala Ala Arg Gly Met Gly Asp Arg Met 465 470 475 480
Asn Lys Ser Leu Ala Ala Gly Gly Pro Ala Pro Lys Ala Ala Pro Lys 485 490 495

Lys Gly Leu Glu Gly Tyr Phe

500

<210> 67

<211> 279

<212> DNA

<213> Cenarchaeum symbiosum

<220>

<221> CDS

<222> (1)...(279)

<400> 67

atg gcg gac aag ata aag tgc tcg cac ata ctg gta aaa aag cag ggc
Met Ala Asp Lys Ile Lys Cys Ser His Ile Leu Val Lys Lys Gln Gly
1 5 10 15

gag gcg ctc gca gtg caa gag cgc ctc aag gcg ggc gaa aag ttt gga 96
Glu Ala Leu Ala Val Gln Glu Arg Leu Lys Ala Gly Glu Lys Phe Gly
20 25 30

aag ctg gca aag gag ctc tcg ata gac ggg ggc agc gca aag agg gac
Lys Leu Ala Lys Glu Leu Ser Ile Asp Gly Gly Ser Ala Lys Arg Asp

ggc agc ttg ggc tac ttt ggc agg ggc aag atg gta aag ccg ttt gag

Gly Ser Leu Gly Tyr Phe Gly Arg Gly Lys Met Val Lys Pro Phe Glu

50 55 60

gat gcc gcg ttc cgc ctg cag gta ggc gag gta tcc gag ccg gta aaa 240 Asp Ala Ala Phe Arg Leu Gln Val Gly Glu Val Ser Glu Pro Val Lys 65 70 75 80

tcc gag ttt ggc tac cac gtg ata aag cgc ctg gga taa 279 Ser Glu Phe Gly Tyr His Val Ile Lys Arg Leu Gly * 85

<210> 68

<211> 92

<212> PRT

<213> Cenarchaeum symbiosum

<400> 68

 Met
 Ala
 Asp
 Lys
 Ile
 Lys
 Cys
 Ser
 His
 Ile
 Leu
 Val
 Lys
 Gln
 Gly
 Ile
 Leu
 Val
 Lys
 Lys
 Ala
 Lys
 Phe
 Gly
 Arg
 Leu
 Lys
 Ala
 Gly
 Glu
 Lys
 Phe
 Gly
 Arg
 Leu
 Lys
 Ala
 Lys
 Phe
 Gly
 Arg
 Gly
 Lys
 Met
 Val
 Lys
 Pro
 Phe
 Glu

 Asp
 Ala
 Ala
 Ala
 Phe
 Arg
 Leu
 Gly
 Gly
 Lys
 Met
 Val
 Lys
 Pro
 Phe
 Glu

 Asp
 Ala
 Ala
 Ala
 Phe
 Arg
 Leu
 Gly
 Gly
 Gly
 Wal
 Ser
 Glu
 Pro
 Val
 Lys

 Asp
 Ala
 Ala
 Ala
 Phe
 Arg
 Leu
 Gly
 Gly
 Gly
 Wal
 Ser
 Glu
 Pro
 Val
 Lys

 Asp
 Ala
 Ala
 Ala
 Phe
 A

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Ser Glu Phe Gly Tyr His Val Ile Lys Arg Leu Gly 85 90

<210> 69

<211> 402

<212> DNA

<213> Cenarchaeum symbiosum

<220>

<221> CDS

<222> (1)...(402)

<400> 69

atg tct ttg tat ttt acg ata aag acg gcc aac ctg gcc ctg ccc gac

Met Ser Leu Tyr Phe Thr Ile Lys Thr Ala Asn Leu Ala Leu Pro Asp

1 5 10 15

gtg gta aag agg tac aac cac gtc ctg gcg tgc aag agc gag gtg atg 96 Val Val Lys Arg Tyr Asn His Val Leu Ala Cys Lys Ser Glu Val Met 20 25 30

agg gcc gag aag cag atc cag gtg tcc atc tcg tcg ggc ggt ctg

Arg Ala Glu Lys Gln Ile Gln Val Ser Ile Ser Ser Ser Gly Gly Leu

35

40

45

gac aag tac gcg gag ctc aag cag cag ttc aac tcg agg ata acc gag
Asp Lys Tyr Ala Glu Leu Lys Gln Gln Phe Asn Ser Arg Ile Thr Glu
50 55 60

ttc tac cgc tcg ata gag gag ctg gag aag acg ggc gtg gtg gtc aag

Phe Tyr Arg Ser Ile Glu Glu Leu Glu Lys Thr Gly Val Val Lys

65 70 75 80

agc ata gac gag ggg ctc ctg gac ttt ccc gca aag cgc ttt ggg gac 288 Ser Ile Asp Glu Gly Leu Leu Asp Phe Pro Ala Lys Arg Phe Gly Asp

gac atc tgg ctg tgc tgg aag gtg ggc gag cgc gag atc aag ttc tgg 336
Asp Ile Trp Leu Cys Trp Lys Val Gly Glu Arg Glu Ile Lys Phe Trp
100 105 110

cat gaa aag gac tcg ggg ttt gac gga aga aag ccc ata gag gta agt
His Glu Lys Asp Ser Gly Phe Asp Gly Arg Lys Pro Ile Glu Val Ser
115 120 125

gac gag tca cta gtg tag 402
Asp Glu Ser Leu Val *
130

<210> 70

<211> 133

<212> PRT

<213> Cenarchaeum symbiosum

<400> 70

Met Ser Leu Tyr Phe Thr Ile Lys Thr Ala Asn Leu Ala Leu Pro Asp
1 5 10 15

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Val Val Lys Arg Tyr Asn His Val Leu Ala Cys Lys Ser Glu Val Met 25 Arg Ala Glu Lys Gln Ile Gln Val Ser Ile Ser Ser Ser Gly Gly Leu 40 Asp Lys Tyr Ala Glu Leu Lys Gln Gln Phe Asn Ser Arg Ile Thr Glu Phe Tyr Arg Ser Ile Glu Glu Leu Glu Lys Thr Gly Val Val Lys 70 75 Ser Ile Asp Glu Gly Leu Leu Asp Phe Pro Ala Lys Arg Phe Gly Asp 90 Asp Ile Trp Leu Cys Trp Lys Val Gly Glu Arg Glu Ile Lys Phe Trp 105 His Glu Lys Asp Ser Gly Phe Asp Gly Arg Lys Pro Ile Glu Val Ser 115 120 Asp Glu Ser Leu Val 130 <210> 71 <211> 879 <212> DNA <213> Cenarchaeum symbiosum <220> <221> CDS <222> (1) ... (879) <400> 71 atg etc tec tec tgg etg ege gta ata ege gte egg tte etg etc geg 48 Met Leu Ser Ser Trp Leu Arg Val Ile Arg Val Arg Phe Leu Leu Ala teg gtg ata gee gta tea geg gge ett gee etc tee tgg tgg eac gge 96 Ser Val Ile Ala Val Ser Ala Gly Leu Ala Leu Ser Trp Trp His Gly cac gga ata gac geg etc aca geg gca etc acc atg gee gga gtg gee 144 His Gly Ile Asp Ala Leu Thr Ala Ala Leu Thr Met Ala Gly Val Ala get ett cat gea age gtg gae atg ete aac gae tae tgg gae tae aag 192 Ala Leu His Ala Ser Val Asp Met Leu Asn Asp Tyr Trp Asp Tyr Lys 55 cgc ggc ata gat acg aga acc aag agg acc ccg atg agc ggg ggg aca 240 Arg Gly Ile Asp Thr Arg Thr Lys Arg Thr Pro Met Ser Gly Gly Thr 65 ggg gtg ctg cca gag ggc ctg ctg agc ccc cgc cag gtg tac cgc gcc 288 Gly Val Leu Pro Glu Gly Leu Leu Ser Pro Arg Gln Val Tyr Arg Ala 85 ggc atc ata tca ctg gtg ctc ggg act gcc gcc gcc gca tac ttt gtg 336 Gly Ile Ile Ser Leu Val Leu Gly Thr Ala Ala Gly Ala Tyr Phe Val 100 105 atc aca acg ggg ccc gtc ata gct gcg ata ctc ggc ttt gcg gtg qtc 384 Ile Thr Thr Gly Pro Val Ile Ala Ala Ile Leu Gly Phe Ala Val Val 115 120

_		Tyr			_					_	_	Gly			gag Glu	432	2
		_	gj y ggg	_	_			_		_			_		tac Tyr 160	480)
	_		ccc Pro	_		_			-			_			_	528	ł
		_	ctg Leu 180									_		_	_	576	,
	_		gac Asp	_		-		_		_	_				_	624	
			agg Arg													672	
			gtg Val													720	
			atg Met													768	
			aaa Lys 260									Arg				816	
			cgg Arg			Arg	Thr		Gly	Ala	Leu					864	
			ggt Gly					_								879	
	. 7	10.	70														
		10> 11>															
		12>															
	<2	13>	Cena	rcha	eum .	symb	iosu	m									

<400> 72

 Met
 Leu
 Ser
 Trp
 Leu
 Arg
 Val
 Ile
 Arg
 Phe
 Leu
 Ala
 Ala

 1
 5
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 10
 10
 15
 15

 Ser
 Val
 Ile
 Ala
 Val
 Ser
 Ala
 Gly
 Leu
 Ala
 Leu
 Ser
 Trp
 Trp
 His
 Gly

 His
 Gly
 Ile
 Asp
 Ala
 Leu
 Thr
 Ala
 Ala
 Leu
 Thr
 Met
 Ala
 Gly
 Val
 Ala

 35
 40
 40
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Ala Leu His Ala Ser Val Asp Met Leu Asn Asp Tyr Trp Asp Tyr Lys 55 Arg Gly Ile Asp Thr Arg Thr Lys Arg Thr Pro Met Ser Gly Gly Thr Gly Val Leu Pro Glu Gly Leu Leu Ser Pro Arg Gln Val Tyr Arg Ala 90 Gly Ile Ile Ser Leu Val Leu Gly Thr Ala Ala Gly Ala Tyr Phe Val 105 Ile Thr Thr Gly Pro Val Ile Ala Ala Ile Leu Gly Phe Ala Val Val 120 Ser Ile Tyr Phe Tyr Ser Thr Arg Ile Val Asp Ser Gly Leu Ser Glu 135 Val Leu Val Gly Val Lys Gly Ala Met Ile Val Leu Gly Ala Tyr Tyr 150 Ile Gln Ala Pro Glu Ile Thr Pro Ala Ala Leu Leu Val Gly Ala Ala 170 Val Gly Ala Leu Ser Ser Ala Val Leu Phe Val Ala Ser Phe Pro Asp His Asp Ala Asp Lys Glu Arg Gly Arg Lys Thr Leu Val Ile Ile Leu 200 Gly Lys Lys Arg Ala Ser Arg Ile Leu Trp Val Phe Pro Ala Val Ala 215 220 Tyr Ser Ser Val Ile Ala Gly Val Ile Ile Gln Val Leu Pro Val Tyr 230 235 Ser Leu Ala Met Leu Leu Ala Ala Pro Leu Ala Ala Ile Ser Ala Arg 250 Gly Leu Ala Lys Glu Tyr Asp Gly Asp Arg Ile Ile Arg Val Met Arg 265 Gly Thr Leu Arg Phe Ser Arg Thr Ala Gly Ala Leu Leu Val Leu Gly 275 280 Ile Leu Leu Gly 290 <210> 73 <211> 1227 <212> DNA <213> Cenarchaeum symbiosum <220> <221> CDS <222> (1)...(1227) <400> 73 ttg agg ccc gcg gct gtg cct aca gca cgg gat att ggc gca gaa cgg 48 Met Arg Pro Ala Ala Val Pro Thr Ala Arg Asp Ile Gly Ala Glu Arg 1 ggc aat ctc aca ctt tgt acc ctt cat aca cat aaa tcc cgc ttg gat 96 Gly Asn Leu Thr Leu Cys Thr Leu His Thr His Lys Ser Arg Leu Asp gtg cgg ctg cgc atg atc agc ggg cat gcc acg gcc gag ggt aca cag 144 Val Arg Leu Arg Met Ile Ser Gly His Ala Thr Ala Glu Gly Thr Gln 40 agg ata gcc gag atg tcc ggc gca cac cat gac aac tac aag gtg gta 192 Arg Ile Ala Glu Met Ser Gly Ala His His Asp Asn Tyr Lys Val Val 55 60

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_	-	_							_						gac Asp 80	240
	gat Asp	_	_		_		_	-		-		_	_			288
	aag Lys	_				_		_						_		336
_	agg Arg	_		-												384
	999 Gly 130	_	_			_	_						_			432
	gtg Val															480
	aag Lys	-		_				_		_			-			528
_	gga Gly			-	_	_						-	_		_	576
_	agc Ser		_		_		_	_	-		-		_			624
	aac Asn 210	_				_		_	_	-			-			672
	gag Glu					_					_		_			720
	ggc Gly												_			768
_	gca Ala			_	_	_	-	_	_		_	_		_		816
	gcc Ala															864
ctg	cca	ttc	aac	cag	tac	ttt	gac	cag	gcc	tac	atg	gta	aag	aac	cag	912

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Leu	Pro 290		Asn	Gln	Tyr	Phe 295	Asp	Gln	Ala	Tyr	Met 300	Val	Lys	Asn	Gln	
	acg Thr				_				_			_	_		ctg Leu 320	960
_	att Ile					_	_	_		_	_		_	_		1008
	cct Pro		_	_	_								_	_		1056
	ctg Leu	_						_				_			_	1104
	cac His 370	_		_	_			_				_		_	J J	1152
	ccc Pro			Pro		_	_						_	_		1200
	tca Ser		Ser			_		tag *								1227

<210> 74

<211> 408

<212> PRT

<213> Cenarchaeum symbiosum

<400> 74

Met Arg Pro Ala Ala Val Pro Thr Ala Arg Asp Ile Gly Ala Glu Arg 10 Gly Asn Leu Thr Leu Cys Thr Leu His Thr His Lys Ser Arg Leu Asp 25 Val Arg Leu Arg Met Ile Ser Gly His Ala Thr Ala Glu Gly Thr Gln 40 Arg Ile Ala Glu Met Ser Gly Ala His His Asp Asn Tyr Lys Val Val Asp Gly Leu His Leu Ser Asn Val Gly Met Gly Thr Tyr Leu Gly Asp 75 Ala Asp Asp Ala Thr Asp Arg Ala Val Thr Asp Ala Val Lys Arg Ser 90 Ile Lys Ser Gly Ile Asn Val Ile Asp Thr Ala Ile Asn Tyr Arg Leu 105 Gln Arg Ala Glu Arg Ser Val Gly Arg Ala Val Thr Glu Leu Ser Glu 120 125 Glu Gly Leu Val Ser Arg Asp Gln Ile Phe Ile Ser Thr Lys Ala Gly 135 140 Tyr Val Thr Asn Asp Ser Glu Val Ser Leu Asp Phe Trp Glu Tyr Val 150 155 160

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Lys Lys Glu Tyr Val Gly Gly Val Ile Gln Ser Gly Asp Ile Ser

170 Ser Gly Tyr His Cys Met Lys Pro Ala Tyr Leu Glu Asp Gln Leu Lys 185 Arg Ser Leu Ala Asn Met Asn Val Asp Cys Ile Asp Leu Val Tyr Val 200 His Asn Pro Val Glu Gly Gln Ile Lys Asp Arg Pro Val Pro Glu Ile 215 220 Leu Glu Gly Ile Gly Glu Ala Phe Ala Met Tyr Glu Lys Met Arg Glu 230 235 Ala Gly Arg Ile Arg Tyr Tyr Gly Leu Ala Thr Trp Glu Cys Phe Arg 245 250 Val Ala Glu Gly Asp Pro Gln Ser Met Gln Leu Glu Ala Val Lys 260 265 Lys Ala Lys Asp Ala Gly Gly Glu Asn His Gly Phe Arg Phe Ile Gln Leu Pro Phe Asn Gln Tyr Phe Asp Gln Ala Tyr Met Val Lys Asn Gln Gly Thr Gly Gly Lys Ser Ser Ile Leu Glu Ala Ala Ala Leu 310 315 Asp Ile Gly Val Phe Thr Ser Val Pro Phe Met Gln Gly Lys Leu Leu 330 Glu Pro Gly Leu Leu Pro Glu Phe Gly Gly Leu Ser Pro Ala Leu Arg 345 Ser Leu Gln Phe Ile Arg Ser Thr Pro Gly Val Leu Ala Pro Leu Pro 360 Gly His Lys Ser Ser Leu His Thr Asp Glu Asn Leu Lys Ile Met Gly 375 380 Val Pro Pro Ile Pro Pro Asp Lys Phe Gly Glu Leu Val Ala Ser Leu 390 Thr Ser Trp Ser Pro Gly Gln Lys 405 <210> 75 <211> 1077 <212> DNA <213> Cenarchaeum symbiosum <220> <221> CDS <222> (1)...(1077) <400> 75 atg aac aac egg ttc cag gtt atc egg ggg gat gee egg geg gtg etg 48 Met Asn Asn Arg Phe Gln Val Ile Arg Gly Asp Ala Arg Ala Val Leu 1 eec agg ett gea aaa aag aat gge gag ege gge agg tae agg etg gee 96 Pro Arg Leu Ala Lys Lys Asn Gly Glu Arg Gly Arg Tyr Arg Leu Ala gtc act tcc ccc ccg tat tac ggg cac aga aag tac ggg tcg gat ccc 144 Val Thr Ser Pro Pro Tyr Tyr Gly His Arg Lys Tyr Gly Ser Asp Pro 40 tee gag etg gge cag gag ggg acg eet gat gag tte gte gag gag etg 192 Ser Glu Leu Gly Gln Glu Gly Thr Pro Asp Glu Phe Val Glu Glu Leu 55 60

_				_	_	tgc Cys	_	_	_			-	_		_	240
						gac Asp					_		_	_	•	288
_	_					ctc Leu										336
		-		_		tac Tyr	_						_	-	_	384
_	_			_	_	gcg Ala 135					_				_	432
_	_			_		gac Asp		-	_		_	_	_			480
	_	_	_		_	aac Asn		_	_		_	-		_	Gln	528
						gac Asp		_	_					_	-	576
				_		ccc Pro		_	_		_		_			624
				_		gcc Ala 215				_		_	_		_	672
_		-		-	_	ttc Phe					_	_	_			720
						ccg Pro										768
_					_	tgg Trp					_					816
						ttc Phe					-				-	864
aag	ttt	gcc	aca	aga	gag	ggc	gac	tat	gtg	ctg	gat	ccg	ttt	gcg	gga	912

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Lys Phe Ala Thr Arg Glu Gly Asp Tyr Val Leu Asp Pro Phe Ala Gly 295

agg ggc aca acg ggg ata gtc tcg gcg tgc ctc aag agg ggc ttt acg 960 Arg Gly Thr Thr Gly Ile Val Ser Ala Cys Leu Lys Arg Gly Phe Thr 310 315

gga ata gac ctg tat cct gcc aac gtg gac agg acc cgg cgc aat gtg 1008 Gly Ile Asp Leu Tyr Pro Ala Asn Val Asp Arg Thr Arg Arg Asn Val 325 330

aaa gat tet geg gae teg aag etg eea aaa aag gtg eta gae eag ata 1056 Lys Asp Ser Ala Asp Ser Lys Leu Pro Lys Lys Val Leu Asp Gln Ile 340 345

atg ccc gag gga aca cgc tga 1077 Met Pro Glu Gly Thr Arg * 355

<210> 76

<211> 358

<212> PRT

<213> Cenarchaeum symbiosum

<400> 76 Met Asn Asn Arg Phe Gln Val Ile Arg Gly Asp Ala Arg Ala Val Leu Pro Arg Leu Ala Lys Lys Asn Gly Glu Arg Gly Arg Tyr Arg Leu Ala 25 Val Thr Ser Pro Pro Tyr Tyr Gly His Arg Lys Tyr Gly Ser Asp Pro 40 Ser Glu Leu Gly Gln Glu Gly Thr Pro Asp Glu Phe Val Glu Glu Leu Ala Gly Val Phe Lys Ser Cys Met Asp Leu Leu Thr Asp Asp Gly Ser 70 Leu Phe Ile Val Ile Gly Asp Thr Arg Arg Arg Arg Lys Leu Met 90 Val Pro His Arg Leu Ala Leu Arg Leu Val Asp Leu Gly Tyr His Phe 105 Gln Glu Asp Ile Val Trp Tyr Lys Lys Asn Ala Leu Ser Gln Ser Ser 120 125 Lys Gln Asn Leu Thr Gln Ala Tyr Glu Phe Val Leu Val Leu Ser Lys 135 Ser Glu Ser Pro Ala Phe Asp Ile Asp Pro Ile Arg Val Gln Gly Asn 150 155 Glu Ala Leu Ser Gly Val Asn Arg Lys Pro Glu Arg Asp Arg Leu Gln 170 Phe Ser Pro Gly Arg Arg Asp Pro Glu Ala Ile Gly Arg Ile Ala Ala 185 Val Ile His Gly Ser Ser Pro Glu Thr Pro Phe Asp Glu Leu Pro Thr 200 205 Thr Glu Glu Ile Ser Arg Ala His Gly Tyr Asp Pro Glu Lys His Cys 215

Pro Thr Cys Tyr Arg Lys Phe Lys Arg His Ala Thr Arg Lys Arg Ile

Gly Gly His Glu His Tyr Pro Ile Phe Ala Ala Cys Asn Pro Arg Gly

235

250

230

245

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Lys	Asn	Pro	Gly 260		Val	Trp	Glu	11e 265		Thr	Lys	Ala	His 270		Gly	
Asn	Glu	His 275		Ala	Val	Phe	Pro 280		Asp	Lev	val	Ser 285	_	Ile	Val	
Lys	Phe 290		Thr	Arg	Glu	Gly 295	Asp	Tyr	Val	Leu	Asp 300		Phe	Ala	Gly	
Arg	Gly	Thr	Thr	Gly	Ile	Val	Ser	Ala	Cys	Leu	Lys	Arg	Gly	Phe	Thr	
305					310					315					320	
				325		Ala			330			_		335		
Lys	Asp	Ser	Ala 340	qeA	Ser	Lys	Leu	Pro 345	Lys	Lys	Val	Leu	Asp 350	Gln	Ile	
Met	Pro	Glu 355	Gly	Thr	Arg											
	<:	210>	77						-							•
	<:	211>	468													
	<:	212>	DNA													
	<:	213>	Cena	arch	aeum	symb	oiosı	am.								
	<:	220>														
	<:	221>	CDS				•									
	<2	222>	(1)	(4	468)											
	<4	100>	77													
atg	cgg	ctg	ccc	cgg	cgc	cga	ctt	aaa	atc	gtt	gta	gga	tgc	ggc	gcc	48
Met	Arg	Leu	Pro	Arg	Arg	Arg	Leu	Lys	Ile	Val	Val	Gly	Cys	Gly	Ala	
1				5					10					15		
gca	gat	gca	ttg	ccc	gcc	tta	tac	acc	gcc	cgg	gat	cgg	ccg	cct	tgc	96
Ala	Asp	Ala		Pro	Ala	Leu	Tyr	Thr	Ala	Arg	Asp	Arg	Pro	Pro	Cys	
			20					25					30			
agc	aca	cgc	agt	ata	aac	999	ggc	ccg	ggc	ggc	gcg	tat	cac	atg	tgg	144
						Gly										
		35					40			٠		45				
ata	aag	gac	gaa	ttc	ctc	ggc	ccg	ggc	aac	aag	atg	agg	ctg	ctc	tac	192
Ile	Lys	qaA	Glu	Phe	Leu	Gly	Pro	Gly	Asn	Lys	Met	Arg	Leu	Leu	Tyr	
	50					55					60					
ctq	ata	cta	ccc	atc	tat	ggg	tat	atc	ttt	cta	gag	tac	tat	cca	ttc	240
						Gly										210
65					70	•	-			75		-	•		80	
ttt	ccc	taa	atα	acc	acc	tac	taa	taa	tca	σta	act	ctc	200	ccc	cca	288
						Tyr										200
		•		85		-2-			90					95		
				_												
						gcc										336
тте	val	FLO		HIS	Tyr	Ala	GIA		Ala	Leu	GLY			Ile	GIy	
			100					105					110			
gat	cac	gta	ttg	ttt	ggc	atc	acc	aca	aag	tac	gtc	tat	gcq	gca	ata	384
						Ile										-
		115					120					125				
tgg	ctc	ggc	atg	gcc	cat	999	ata	atc	ctg	ctg	gca	9 99	cgc	ctc	cgg	432
									-	_					-	

468

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Trp Leu Gly Met Ala His Gly Ile Ile Leu Leu Ala Gly Arg Leu Arg
130

gga cct agg cag gcg cca cgg acg ggc atc cca tag
Gly Pro Arg Gln Ala Pro Arg Thr Gly Ile Pro *
145

<210> 78

<211> 155 <212> PRT <213> Cenarchaeum symbiosum

<400> 78

Met Arg Leu Pro Arg Arg Leu Lys Ile Val Val Gly Cys Gly Ala Ala Asp Ala Leu Pro Ala Leu Tyr Thr Ala Arg Asp Arg Pro Pro Cys Ser Thr Arg Ser Ile Asn Gly Gly Pro Gly Gly Ala Tyr His Met Trp 40 Ile Lys Asp Glu Phe Leu Gly Pro Gly Asn Lys Met Arg Leu Leu Tyr Leu Ile Leu Pro Ile Tyr Gly Tyr Ile Phe Leu Glu Tyr Tyr Pro Phe Phe Pro Trp Met Ala Thr Tyr Trp Trp Ser Val Ala Leu Ser Pro Pro 85 90 Ile Val Pro Thr His Tyr Ala Gly Glu Ala Leu Gly Arg Leu Ile Gly 105 Asp His Val Leu Phe Gly Ile Thr Thr Lys Tyr Val Tyr Ala Ala Ile 120 Trp Leu Gly Met Ala His Gly Ile Ile Leu Leu Ala Gly Arg Leu Arg 135 Gly Pro Arg Gln Ala Pro Arg Thr Gly Ile Pro 150

<210> 79
<211> 1779
<212> DNA
<213> Cenarchaeum symbiosum
<220>
<221> CDS

.400

<222> (1)...(1779)

ttg aag ctg caa ggc aag act gcc gtg atc acc ggc agt ggt acc ggg 48

Met Lys Leu Gln Gly Lys Thr Ala Val Ile Thr Gly Ser Gly Thr Gly

1 5 10 15

atc ggg ctg gcg gtg gca agg aaa ttt gcc gag aac ggg gcc agc gtg 96

Ile Gly Leu Ala Val Ala Arg Lys Phe Ala Glu Asn Gly Ala Ser Val

20 25 30

gta ata ctc gga agg aga aag gag ccc ctc gat gag gca gca gca gag

Yal Ile Leu Gly Arg Arg Lys Glu Pro Leu Asp Glu Ala Ala Ala Glu

45

ctc aaa aag ata gcg gaa tct gca ggc tgc ggg gcc tcg atc agg ata 192

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Leu	Lys 50	Lys	Ile	Ala	Glu	Ser 55	Ala	Gly	Cys	Gly	Ala 60	Ser	Ile	Arg	Ile	
				-	-							acg Thr				240
												ctg Leu				288
_			_			_	_	-		_		aat Asn	_		-	336
		-		_	_	_						tcc Ser 125				384
												aag Lys				432
_		_			•	_						cag Gln		_		480
		-	_	_				_	_		_	aag Lys				528
-	-		_									ata Ile				576
						_			_			tac Tyr 205	_	_	-	624
	_			_				-		_		Gly ggg			_	672
												cta Leu				720
												gca Ala				768
												aag Lys				816
		_	_	_		_	_		_			gcc Ala 285	_	_		864

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G	ag ln	gcc Ala 290	aac Asn	act Thr	gca Ala	agg Arg	atg Met 295	ata Ile	cca Pro	gac Asp	gjå aaa	gag Glu 300	ttt Phe	ctc Leu	tcc Ser	cag Gln	912
A						acg Thr 310											960
a	ag ys	acg Thr	gta Val	aac Asn	ggc Gly 325	cgc Arg	gta Val	atc Ile	ccc Pro	gcc Ala 330	gac Asp	agg Arg	gta Val	ttc Phe	tac Tyr 335	ccg Pro	1008
9 V	ta al	agg Arg	gcg Ala	cat His 340	gtg Val	gcc Ala	aat Asn	gcc Ala	gct Ala 345	ccg Pro	cgc Arg	gtg Val	ccc Pro	ccg Pro 350	cac His	gac Asp	1056
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						acc Thr											1152
G						ata Ile 390											1200
						aag Lys											1248
						agg Arg											1296
						gtc Val											1344
						tcc Ser											1392
P						gct Ala 470											1440
						aag Lys											1488
						ggc Gly											1536
9	gc	gcc	gag	agg	gca	agg	gcg	gag	atc	ttc	cgg	ggt	gcg	ctc	agg	ccg	1584

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Leu Gln Pro Glu Glu Val Glu Val Ala Gly Gly Arg Leu Ile His Leu

230

235

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Glu His Phe Ala Lys Leu Lys Pro Val Asp Pro Ala Lys Leu Glu Ala
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Thr Leu Asp Ala Leu Leu Ala Lys Ile Lys Gly Ile Ala Glu Lys Ile
                           280
Gln Ala Asn Thr Ala Arg Met Ile Pro Asp Gly Glu Phe Leu Ser Gln
                      295
Asp Gln Val Ala Glu Thr Val Leu Ala Leu Cys Asp Asp Lys Met Ala
                   310
                                      315
Lys Thr Val Asn Gly Arg Val Ile Pro Ala Asp Arg Val Phe Tyr Pro
                                  330
               325
Val Arg Ala His Val Ala Asn Ala Ala Pro Arg Val Pro Pro His Asp
           340
                              345
Tyr Ser Gly Gly Cys Val Leu Phe Met Ile Asp Ala Ala Asp Asp Arg
                           360
Asp Val Glu Arg Ala Thr Ala Leu Ala Ser His Val Glu Ser His Gly
                       375
Gly Thr Ala Val Cys Ile Val Ser Glu Asp Ser Pro Arg Ala Ala Lys
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                           395
Glu Met Ile Ala Ser Lys Phe His Ser His Ala Ser His Ile Asp Lys
                    410
Val Asp Glu Ile Asn Arg Trp Leu Ser Ala Ala Ser Thr Lys Ile Gly
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Pro Ile Ser Ala Val Val His Leu Ser Gly Arg Met Pro Lys Ser Gly
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Ser Leu Met Asp Leu Ser Arg Lys Glu Trp Asp Ala Leu Val Asp Arg
                      455
                                          460
Phe Ile Gly Thr Pro Ala Ala Val Leu His Arg Ser Leu Glu His Phe
                  470
                                      475
Ala Pro Gly Gly Arg Lys Asp Pro Arg Leu Phe Lys Gly Lys Ser Gly
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Val Ile Val Ile Ile Gly Pro Asp Leu Pro Ala Gly Lys Lys Ala Ser
                              505
Gly Ala Glu Arg Ala Arg Ala Glu Ile Phe Arg Gly Ala Leu Arg Pro
                          520
Leu Thr Thr Thr Val Asn Gln Glu Leu Ser Asp Val Leu Lys Ser Asn
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                                          540
Val Arg Leu Phe Thr Ile Leu Pro Gly Arg Ala Asp Gly Glu Thr
Asp Asp Ser Arg Ile Ser Ala Ala Ile Asp Tyr Phe Leu Thr Pro Glu
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42

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ataccgagaa gttatagcag ggtatggaat gtgcgcgcgc atg
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egegeggeee geetgetgeg eagatetgte egteeageet gatgtgggge aggeaacatg
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а
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cacagaatga gggtatgatc gaagggtcat atctgagatg tgaagattat gtgcattctg
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                                                                    120
cacagaatga ggatctgatc gaagggtcat atctgagatg tgaagattat gtgcattccg
                                                                    180
ttcaattcca aaagtacagg cgtactttga aaaaaaaaat aatccaaata agaat
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